F.T. Alexandra Mahaney, State Bar No. 125984
Natalie J. Morgan, State Bar No. 211143
WILSON SONSINI GOODRICH & ROSATI
Professional Corporation
12235 El Camino Real, Suite 200
San Diego, CA 92130
Telephone: (858) 350-2300
Facsimile: (858) 350-2399
Email: amahaney@wsgr.com
Email: nmorgan@wsgr.com

Bruce R. Genderson (admitted *pro hac vice*)
Aaron P. Maurer (admitted *pro hac vice*)
Rachel Shanahan Rodman (admitted *pro hac vice*)
Adam D. Harber (admitted *pro hac vice*)
WILLIAMS & CONNOLLY LLP
725 Twelfth St. NW
Washington, DC 20005
(202) 434-5000

Attorneys for Defendant and Counterclaimant
SENORX, INC.

IN THE UNITED STATES DISTRICT COURT

NORTHERN DISTRICT OF CALIFORNIA

SAN JOSE DIVISION

HOLOGIC, INC., CYTYC CORPORATION and HOLOGIC L.P., Plaintiffs, v. SENORX, INC., Defendant. AND RELATED COUNTERCLAIMS	CASE NO.: C08-0133 RMW (RS) **DECLARATION OF ADAM D. HARBER IN SUPPORT OF DEFENDANT SENORX, INC.'S OPPOSITION TO PLAINTIFFS' MOTION FOR A PRELIMINARY INJUNCTION -- SUBMITTED PURSUANT TO PERMISSION GRANTED AT HEARING OF APRIL 21, 2008** Date: April 21, 2008 Time: 2:00 p.m. Courtroom: 6, 4th Floor Judge: Hon. Ronald M. Whyte

I, Adam D. Harber, declare as follows:

1. I am an associate at the law firm Williams & Connolly LLP, admitted pro hac vice to practice before this Court in the above-captioned matter. I serve as one of the outside counsel for Defendant SenoRx, Inc. ("SenoRx"). The following declaration is based on my personal knowledge, and if called upon to testify, I could and would competently testify as to the matters set forth herein.

2. Attached hereto as Exhibit 31[1] is a true and correct copy of excerpts of the deposition of Lynn Verhey. In particular, the excerpts include:

a. pages 80-81 (cited in '204 Patent Invalidity Presentation, slide 22) (re: Ashpole);

b. pages 57-58 (cited in '204 Patent Invalidity Presentation, slide 28) (re: Ashpole);

c. pages 105-06 (cited in '204 Patent Invalidity Presentation, slide 35 and 41) (re: Ashpole);

d. pages 109-10 (cited in '204 Patent Invalidity Presentation, slides 37 and 39) (re: Ashpole);

e. pages 97-98 (cited in '204 Patent Invalidity Presentation, slide 44) (re: Ashpole);

f. pages 104-105 (cited in '204 Patent Invalidity Presentation, slide 45) (re: Ashpole);

g. pages 94-95 (cited in '204 Patent Invalidity Presentation, slide 48) (re: Ashpole);

h. page 76 (cited in '204 Patent Invalidity Presentation, slide 50) (re: Ashpole);

[1] The numbers assigned to exhibits attached to this Declaration run consecutively from the exhibit numbers of those attached to the Declaration of Aaron P. Maurer in Support of Defendant SenoRx, Inc.'s Opposition to Plaintiffs' Motion for a Preliminary Injunction.

i. page 88 (cited in '204 Patent Invalidity Presentation, slide 52) (re: Ashpole);

j. pages 22-26 (cited in '204 Patent Invalidity Presentation, slide 54) (re: radionecrosis);

k. page 131 (cited in '142 Patent Anticipation Presentation, slides 23 and 25) (re: '774 patent);

l. pages 135-36 (cited in '142 Patent Anticipation Presentation, slides 27-28) (re: '774 patent);

m. page 137 (cited in '142 Patent Anticipation Presentation, slides 30, 33, and 34) (re: '774 patent); and

n. page 138 (cited in '142 Patent Anticipation Presentation, slide 35) (re: '774 patent).

3. Attached hereto as Exhibit 32 is a true and correct copy of relevant excerpts of the deposition of Colin Orton. In particular, the excerpts include:

a. pages 34 and 70-73 (cited in '204 Patent Invalidity Presentation, slide 54) (re: radionecrosis);

b. pages 34-36 (cited in '204 Patent Invalidity Presentation, slides 57-58) (re: Ashpole); and

c. page 31 (cited in '204 Patent Invalidity Presentation, slide 59) (re: Ashpole).

4. Attached hereto as Exhibit 33 is a true and correct copy of relevant excerpts of the deposition of Martin Keisch. In particular, the excerpts include:

a. pages 104-05, 108-10 (cited in Remaining Factors Presentation, slide 6) (re: skin pressure); and

b. page 52 (cited in Remaining Factors Presentation, slide 15) (re: promotion of Contura).

5. Attached hereto as Exhibit 34 is a true and correct copy of relevant excerpts of the deposition of Philip Israel. In particular, the excerpts include:

a. pages 123-24 (cited in Remaining Factors Presentation, slide 6) (re: skin pressure);

b. pages 145-46 (cited in Remaining Factors Presentation, slide 7) (re: clinical data); and

c. page 75 (cited in Remaining Factors Presentation, slide 13) (re: Contura warning).

6. Attached hereto as Exhibit 35 is a true and correct copy of relevant excerpts of the deposition of Douglas Arthur. In particular, the excerpts include:

a. page 68 (cited in Remaining Factors Presentation, slide 13) (re: Contura warning).

7. Attached hereto as Exhibit 36 is a true and correct copy of relevant excerpts of the deposition of Julie Davis. In particular, the excerpts include:

a. pages 237-38 (cited in Remaining Factors Presentation, slide 16) (re: 2009 projections);

b. page 233 (cited in Remaining Factors Presentation, slide 16) (re: SenoRx market value);

c. pages 57-58, 130, 137, 140, and 152-55 (cited in Remaining Factors Presentation, slide 19) (re: price erosion);

d. page 211 (cited in Remaining Factors Presentation, slide 20) (re: Hologic investment in APBI market); and

e. pages 40-41 (cited in Remaining Factors Presentation, slide 20) (re: lost sales).

8. Attached hereto as Exhibit 37 is a true and correct copy of relevant excerpts of the deposition of William Gearhart. In particular, the excerpts include:

a. pages 50-51 (cited in Remaining Factors Presentation, slide 17) (re: Contura pricing).

9. Attached hereto as Exhibit 38 is a true and correct copy of an amendment and response filed on December 20, 2000 in the prosecution history of U.S. Patent No. 6,413,204. In

particular, an excerpt of the first full paragraph of page 16 of Exhibit 38 (the statement regarding "compression of the brain tissue" and "conform[ing] the tissue to the desired shape of the expandable surface element, as is recited in claims 4 and 28") was displayed by Plaintiffs and discussed by both parties.

10. Attached hereto as Exhibit 39 is a true and correct copy of Exhibit 12 of the deposition of Lynn Verhey (cited in '142 Patent Anticipation Presentation, slide 34) (drawing of isodose curves around Figure 3 of the '774 patent).

11. Attached hereto as Exhibit 40 is a true and correct copy of relevant excerpts of Exhibit 6 of the deposition of Julie Davis (cited in Remaining Factors Presentation, slide 16) (internal SenoRx projection for 2009).

12. Attached hereto as Exhibit 41 is a true and correct copy of Exhibit 7 of the deposition of Julie Davis (cited in Remaining Factors Presentation, slide 16) (analyst report projecting SenoRx profit in 2009).

I declare under penalty of perjury that the foregoing is true and correct.

Dated: April 23, 2008

By: _____
Adam D. Harber

CERTIFICATE OF SERVICE
U.S. District Court, Northern District of California, San Jose Division
Hologic, Inc. et al. v. SenoRx, Inc.
Case No. C-08-0133 RMW (RS)

I, Liz Bojorquez, declare:

I am and was at the time of the service mentioned in this declaration, employed in the County of San Diego, California. I am over the age of 18 years and not a party to the within action. My business address is 12235 El Camino Real, Ste. 200, San Diego, CA, 92130.

On April 23, 2008, I served a copy(ies) of the following document(s):

DECLARATION OF ADAM D. HARBER IN SUPPORT OF DEFENDANT SENORX, INC.'S OPPOSITION TO PLAINTIFFS' MOTION FOR A PRELIMINARY INJUNCTION – SUBMITTED PURSUANT TO PERMISSION GRANTED AT HEARING OF APRIL 21, 2008 AND EXHIBITS 31, 32, 34, 35, 38, 39 and 41 THERETO

on the parties to this action by placing them in a sealed envelope(s) addressed as follows:

Henry C. Su (suh@howrey.com) Katharine L. Altemus (altemusk@howrey.com) HOWREY LLP 1950 University Avenue, 4th Floor East Palo Alto, CA 94303 Telephone: (650) 798-3500 Facsimile: (650) 798-3600	Attorneys for Plaintiffs HOLOGIC, INC. CYTYC CORPORATION and HOLOGIC LP
Matthew Wolf (wolfm@howrey.com) Marc Cohn (cohnm@howrey.com) HOWREY LLP 1229 Pennsylvania Avenue, NW Washington, DC 20004 Telephone: (202) 783-0800 Facsimile: (202) 383-6610	Attorneys for Plaintiffs HOLOGIC, INC. CYTYC CORPORATION and HOLOGIC LP

☐ (BY MAIL) I placed the sealed envelope(s) for collection and mailing by following the ordinary business practices of Wilson Sonsini Goodrich & Rosati, 12235 El Camino Real, Ste. 200, San Diego, CA. I am readily familiar with WSGR's practice for collecting and processing of correspondence for mailing with the United States Postal Service, said practice being that, in the ordinary course of business, correspondence with postage fully prepaid is deposited with the United States Postal Service the same day as it is placed for collection.

☒ (BY ELECTRONIC MAIL) I caused such document(s) to be sent via electronic mail (email) to the above listed names and email addresses.

☐ (BY PERSONAL SERVICE) I caused to be delivered by hand to the addressee(s) noted above. I delivered to an authorized courier or driver to be delivered on the same date. A proof of service signed by the authorized courier will be filed with the court upon request.

☐ (BY OVERNIGHT DELIVERY) I placed the sealed envelope(s) or package(s), to the addressee(s) noted above, designated by the express service carrier for collection and overnight delivery by following the ordinary business practices of Wilson Sonsini Goodrich & Rosati, 12235 El Camino Real, Ste. 200, San Diego, CA. I am readily familiar with WSGR's practice for collecting and processing of correspondence for overnight delivery, said practice being that, in the ordinary course of business, correspondence for overnight delivery is deposited with delivery fees paid or provided for at the carrier's express service offices for next-day delivery the same day as the correspondence is placed for collection.

☐ (BY FACSIMILE) I caused to be transmitted by facsimile machine (number of sending facsimile machine is (858) 350-2399 at the time stated on the attached transmission report(s) by sending the documents(s) to (see above). The facsimile transmission(s) was/were reported as complete and without error.

☒ (BY CM/ECF) I caused such document(s) to be sent via electronic mail through the Case Management/Electronic Case File system with the U.S. District Court for the Northern District of California.

I declare under penalty of perjury under the laws of the United States that the above is true and correct, and that this declaration was executed on April 23, 2008.

Liz Bojorquez

Exhibit 31

UNITED STATES DISTRICT COURT
NORTHERN DISTRICT OF CALIFORNIA
SAN JOSE DIVISION

---o0o---

HOLOGIC, INC., CYTYC CORPORATION, and HOLOGIC L.P.,

Plaintiffs,

vs. No. C08 00133 RMW (RS)

SENORX, INC.,

Defendant.

AND RELATED COUNTERCLAIMS.

DEPOSITION OF LYNN VERHEY

San Francisco, California

Wednesday, April 16, 2008

REPORTED BY:
LYNNE LEDANOIS
CSR No. 6811
Job No. 79773

handheld X-ray device for radiating, as an example, lumpectomy sites post surgery.

Q Who makes that handheld radiation source?

A It's actually distributed by Zeiss. It was originally designed and created by a company called Photoelectron Corporation, which was then purchased by Ziess.

Q Is this the device that was at issue in the Xoft case?

A No.

Q Is that device, the Zeiss device, used interstitially --

A Yes.

Q -- or is it an external treatment?

A It's interstitial.

Q When it's used interstitial, is it used in a balloon?

A No.

Q How is it used interstitially?

A They have a series of plastic balls of different diameters which they insert into the surgical cavity; then the X-ray tube goes into a hole inside that.

Q Are these balls expandable or are they fixed in shape?

A Fixed in shape; just a number of different diameters you can use depending on the size of the surgical cavity.

Q What tissues are those used in?

A Breast is the only place that we have used it to date.

Q Are you familiar with the Gliasite device?

A No.

Q Do you know what it is?

A No.

Q Are you familiar with the Contura device?

A I've heard the name, but I don't know the details of it at all. I think it's for similar kinds of radiation.

Q In what context did you hear the name?

A Probably at a meeting.

Q At a meeting about this lawsuit or --

A No, no, no. I'm sorry. At a professional meeting where I typically go around and look at what's new in technology.

Q Do you remember what meeting that was?

A Probably ASTRO.

Q What is ASTRO?

A American Society of Therapeutic Radiation Oncology.

Q Are you a member of ASTRO?

A Yes.

Q Do you know Dr. Orton?

A I do.

Q Do you know his representation in the field?

A Yes.

Q Is he well respected?

A Yes.

Q Would you turn back to Exhibit 1. In particular I'm going to point you to paragraph 10 and 11 where you discuss what's called a person of ordinary skill in the art.

Are you there?

A Yes.

Q And you in these paragraphs offer certain qualifications that this person has; right?

A Right.

Q How did you determine these qualifications?

A I was influenced primarily by the rules for experience required, and education required to sit for the certification exam for the American Board of Radiology.

Q These are the requirements that someone needs in order to be board certified for radiation oncology?

A To sit for the exam, correct, yes.

Q Is that a certification that radiation oncologists obtain or radiation physicists obtain or both?

A The American Board of Radiology provides certification for both groups, but there is a specific one for physicists and a separate one for physicians and radiation oncology.

Q The one that you offer here is the one for physicists; correct?

A Correct.

Q So it's your view that the appropriate lens through which to view these patents is someone who's pretty highly qualified in the area of radiation physics?

MR. SU: Objection, form.

THE WITNESS: Yes.

BY MR. MAURER:

Q How many certified radiation physicists are there in the U.S.?

A I don't know the answer to that.

Q Do you know ballpark?

A I would guess there must be many hundreds for sure.

Q Would the person of ordinary skill, as you have defined that person, be responsible for prescribing a

10:23:36 dose of radiation for therapeutic treatment?
10:23:39 A No.
10:23:40 Q That's because this person is a radiation
10:23:42 oncology physicist like yourself; correct?
10:23:46 A Correct.
10:23:50 Q Would the person of ordinary skill, as you
10:23:52 defined it, be responsible for prescribing the threshold
10:23:58 at which to stay below to avoid radionecrosis?
10:24:02 A No.
10:24:03 Q And, again, that's because they're a radiation
10:24:06 oncologist physicist, not a physician?
10:24:09 A Correct.
10:24:10 Q What is radionecrosis?
10:24:12 A Radionecrosis is radiation-produced cell death.
10:24:20 Q What is the biological mechanism by which it
10:24:23 occurs?
10:24:24 A It would have to do with deposition of energy
10:24:29 from charge particles within the cell which create
10:24:35 openings in one or both strands of DNA, and then when
10:24:40 the cell attempts to multiply, the fact that the DNA has
10:24:47 been damaged will either produce a damaged result or
10:24:50 cell death, which is usually the outcome.
10:24:55 Q Are there different types of radiation
10:24:59 necrosis -- let me ask that a better way.
10:25:02 Is it correct that there is -- acute radiation

10:25:05 necrosis, early-onset radionecrosis and late-developed
10:25:10 radionecrosis are the three categories generally
10:25:14 recognized?
10:25:15 MR. SU: Objection, form.
10:25:18 THE WITNESS: Not precisely.
10:25:19 BY MR. MAURER:
10:25:20 Q Okay.
10:25:22 A There are early and late radiation effects,
10:25:27 which may, in fact, be repairable, and, therefore, not
10:25:36 radionecrosis, but can produce clinical problems,
10:25:40 clinical symptoms which the patient has to suffer
10:25:44 through.
10:25:48 Q Is radionecrosis an early or late radiation
10:25:51 effect?
10:25:53 A It could be either.
10:25:58 Q And is it your understanding that it only shows
10:26:03 up when the cells are attempting to multiply?
10:26:06 A Correct.
10:26:10 Q What are the factors that contribute to whether
10:26:12 or not radionecrosis occurs in a tissue after exposure
10:26:16 to radiation?
10:26:20 A Of course the level of dose, the energy
10:26:25 deposited in the cell is the primary answer to that
10:26:29 question.
10:26:33 Q I'm sorry to interrupt you.

10:26:35 Is level of energy deposited in dose the same
10:26:37 thing?
10:26:38 A Yes.
10:26:39 Q What else, if anything?
10:26:44 A There could be patient-related factors, genetic
10:26:49 factors, for instance, which will make one patient more
10:26:54 sensitive to the same dose of radiation than another
10:26:55 patient.
10:26:57 Q Is that something that would be understood by a
10:26:59 person of ordinary skill in the art?
10:27:01 A It would be understood, yes.
10:27:04 Q What about the dose rate?
10:27:07 A The dose rate is also definitely a factor.
10:27:15 Q What about the volume of tissue that's
10:27:17 radiated?
10:27:18 A The volume of tissue is a factor.
10:27:20 Q Let me go back to the dose rate.
10:27:23 In general terms, how is the dose rate a
10:27:26 factor, higher dose rate lead to more likelihood of
10:27:30 radionecrosis?
10:27:31 A Higher leads to higher probability of
10:27:34 radionecrosis. The reason for that is thought to be
10:27:38 that if you have two radiation-induced DNA events in the
10:27:43 same cell, the period of time which is less than the
10:27:47 time it takes for it to repair the first one, then

10:27:50 you're likely to have radiation necrosis. So the higher
10:27:55 the dose rate, the higher the likelihood of having both
10:27:58 strands damaged.
10:28:02 Q And how does the volume of tissue eradiated
10:28:05 relate to the likelihood of radionecrosis?
10:28:09 A The larger the volume receiving a particular
10:28:11 dose, the likelier of radiation necrosis.
10:28:15 Q Why is that?
10:28:16 A Believe it or not, I think there is some
10:28:18 difference of opinion, but there are situations -- there
10:28:22 are things called bystander phenomenon, where cells
10:28:29 which are not actually eradiated or affected by the
10:28:33 cells neighboring to them which are eradiated.
10:28:37 So there are systemic effects where the
10:28:39 cells -- what's happening to the neighboring cells has
10:28:43 an effect on the cells, even if they have not had much
10:28:45 radiation themselves.
10:28:47 Q And did you say the greater the volume of
10:28:50 tissue that's eradiated, the greater the likelihood
10:28:54 there is radionecrosis?
10:28:57 A Yes.
10:28:57 Q Is one reason for that -- the greater the
10:29:00 volume of tissue eradiated, that means the greater the
10:29:05 number of cells that receive radiation, which, in turn,
10:29:07 means the greater likelihood that one or more of those

Page 26

10:29:10 cells has the DNA damaged?
10:29:12 A Of course.
10:29:18 Q Is the susceptibility of different tissues to
10:29:22 radiation damage different?
10:29:24 A Yes.
10:29:25 Q Why is that?
10:29:28 A It has to do with a lot of biological factors,
10:29:31 including the frequency with which the cells turn over.
10:29:37 So, for instance, cells in the mucosal lining of the
10:29:43 stomach turn over very rapidly, and, therefore, their
10:29:47 damage would be -- they are more susceptible to damage
10:29:53 in cells that don't turn over rapidly, like the
10:29:56 prostate.
10:29:57 Q What about cells in the skin? How susceptible
10:29:59 are they to damage?
10:30:00 A Pretty susceptible, yes.
10:30:02 Q How about cells in the ribs?
10:30:04 A Ribs, not so much.
10:30:05 Q What about in the brain?
10:30:07 A Brain, depends on where you are. But the
10:30:09 answer is basically yes, for most cells in the brain
10:30:16 would have -- would be very sensitive to radiation.
10:30:21 Q There's a couple of different types of cells in
10:30:23 the brain; there's white matter and gray matter, at
10:30:26 least to begin with?

Page 27

10:30:27 A Yes.
10:30:27 Q Which of those two is more susceptible?
10:30:30 A Actually, I'm not sure I know the answer to
10:30:32 that question.
10:30:34 Q If I ask a radiation oncologist, they would
10:30:37 know?
10:30:38 A They would know.
10:30:38 Q Let me hand you what I'll mark as Exhibit 2,
10:31:03 which is the '204 patent.
10:31:05 A Yes.
10:31:05 (Plaintiff's Exhibit 2 was marked for
10:31:05 identification by the Court Reporter.)
10:31:05 BY MR. MAURER:
10:31:12 Q I'm going to ask you to turn to column 6 -- the
10:31:15 column numbers are at the top of the columns -- and in
10:31:19 particular line 53. There is a sentence there that
10:31:28 starts, At high doses of radiation...
10:31:30 Do you see where I am?
10:31:31 A Yes.
10:31:32 Q Can you read that sentence to yourself and
10:31:33 continue through the end of paragraph just so you have
10:31:35 the context?
10:31:56 A Okay.
10:31:58 Q Are the inventors in that section discussing
10:32:00 radionecrosis?

Page 28

10:32:02 A Yes.
10:32:02 Q And what are they talking about when they talk
10:32:05 about the percentage of exposed cells that survive
10:32:10 treatment decreases with first order of kinetics? What
10:32:14 does that -- what is this section describing as would be
10:32:18 understood by a person of ordinary skill in the art?
10:32:21 A To tell you the truth, I'm not sure what they
10:32:25 mean by first order of kinetics. That's not a term
10:32:28 which is familiar to me.
10:32:29 Q For that section as a whole that I just pointed
10:32:32 you to, how would a person of ordinary skill in the art
10:32:36 understand that?
10:32:37 A That it's a very good idea to keep the dose to
10:32:40 the desired range of tissues as low as possible to
10:32:45 minimize radionecrosis.
10:32:47 Q That's standard?
10:32:51 A Yes.
10:32:51 Q That's something any person of ordinary skill
10:32:54 in the art would appreciate?
10:32:56 A Sure.
10:32:56 Q Even without reading it in the patent?
10:32:58 A Yes.
10:32:58 Q Been known for decades?
10:33:01 A Yes, right.
10:33:06 Q Let me talk to you about afterloaders.

Page 29

10:33:06 Does USC -- let me start, do you know what an
10:33:08 afterloader is?
10:33:09 A Yes.
10:33:09 Q What is an afterloader?
10:33:11 A It's a device which can remotely put radiation
10:33:16 source into a catheter that has been inserted into the
10:33:20 patient.
10:33:21 Q Do you know how many afterloaders there are in
10:33:23 the U.S.?
10:33:25 A Large number -- very large number. Probably --
10:33:30 many hundreds, probably more than 1,000, I would guess.
10:33:35 Q When did afterloaders begin to be used in the
10:33:39 U.S.?
10:33:41 A I would say 20 years ago was sort of my first
10:33:47 exposure to them.
10:33:48 Q And for what purpose were they used then?
10:33:53 A Primarily for gynecologic cancer.
10:34:00 Q What was used before afterloaders?
10:34:04 A Sources which are arrayed in a -- as an
10:34:09 example, the catheter, and then placed by hand into the
10:34:14 patient, in the patient cavities, or in some cases
10:34:19 interstitially.
10:34:20 Q And the afterloader is a machine that does
10:34:23 this?
10:34:23 A It does the radiation -- it does the handling

Page 30

10:34:26 of the radiation sources for you remotely, correct.
10:34:30 Q That's favorable because it means like --
10:34:31 people like you are not exposed to radiation all the
10:34:35 time?
10:34:36 A Real good idea, yes.
10:34:37 Q Is there an afterloader or any afterloaders at
10:34:40 UCSF?
10:34:41 A Yes, we have what's called a high dose rate
10:34:43 afterloader.
10:34:44 Q What is that used for?
10:34:45 A Used for a number of things, including
10:34:48 gynecologic tumors, used for tumors in the head and
10:34:53 neck, used for prostate cancer. I guess that would be
10:34:58 the primary application, although there has been some
10:35:03 conversation about using it in local breast cancer.
10:35:09 Q That would be with a device like the MammoSite
10:35:12 or Contura?
10:35:13 A No. The high dose rate afterloader, in fact,
10:35:16 has an individual source which is put into the
10:35:19 catheters. These are not inflatable catheters, simply
10:35:22 catheters that are put in by hand.
10:35:24 Q These are the multicatheter interstitially
10:35:27 placed --
10:35:28 A Exactly, yes.
10:35:35 Q Are afterloaders -- let me try this a different

Page 31

10:35:38 way.
10:35:38 It's true, then, that afterloaders are not
10:35:41 specific to one indication; they can be used for a
10:35:45 number of different things?
10:35:46 A Right.
10:35:48 Q They are just a means of getting radiation into
10:35:54 a body and out of a body?
10:35:54 A Yes.
10:35:55 Q In what form is the radiation source in the
10:36:00 afterloaders that are used today?
10:36:02 A In the one that we have, we have a single
10:36:06 iridium 192 source, which is a very high activity source
10:36:09 with a low half-life, a short half-life of around 90
10:36:14 days, and then it gets replaced every 90 days by the
10:36:20 manufacturer.
10:36:21 Q What do they do with the old ones?
10:36:23 A We have not asked, but probably sent to ***
10:36:26 Hanford, Washington, as a matter of fact, is the
10:36:30 likeliest thing.
10:36:31 Q What shape is the radiation source?
10:36:34 A It's a sphere.
10:36:35 Q A sphere?
10:36:36 A Yes.
10:36:37 Q Attached to the end of the wire?
10:36:39 A Sorry?

Page 32

10:36:39 Q A sphere attached to the end of the wire?
10:36:41 A No. It's -- yes, the end of the wire which
10:36:45 goes -- the guide wire which takes it into the
10:36:47 catheters, yes, that's correct.
10:36:49 Q Let me back up a step.
10:36:51 Can you describe how the radiation source is
10:36:53 inserted into the catheters with the type of afterloader
10:36:56 that UCSF has?
10:36:59 A Yes, the catheter is up to, I believe, 18 of
10:37:07 them are attached to the outlet of a safe in which the
10:37:14 source resides. And then it is programmed to go through
10:37:22 as many of the catheters as are needed for the
10:37:25 particular treatment. And then it is pushed out -- the
10:37:33 wire is pushed out from the safe into the end of the
10:37:37 catheter and then pulled back. And there are dwell
10:37:43 times defined, usually dwell places every 5 millimeters
10:37:48 or so. And the amount of -- number of seconds it spends
10:37:51 at each one of these dwell points is determined by the
10:37:54 treatment plan. And that determines, among other
10:37:57 things, the dose distributed to the patient, the cancer,
10:38:00 and also to the neighboring tissues.
10:38:03 Q Are you sure that the source attached to the --
10:38:06 let me -- who makes your afterloader at UCSF?
10:38:11 A Nucleotron.
10:38:12 Q Are you sure that the source attached to the

Page 33

10:38:13 end of the wire is a sphere as opposed to a cylinder?
10:38:16 A No, actually, I'm not. I have not looked at
10:38:19 it.
10:38:20 Q It could be a cylinder?
10:38:21 A It could be a cylinder.
10:38:22 Q And, in fact, it would make sense if it was a
10:38:26 cylinder because that means they can keep it in the same
10:38:29 diameter with the wire?
10:38:30 MR. SU: Objection, form.
10:38:35 THE WITNESS: It's a logical -- yes.
10:38:45 BY MR. MAURER:
10:38:45 Q When you're using these afterloaders, if there
10:38:47 are dosimetry calculations to be -- well, let me back
10:38:50 up.
10:38:53 Whenever you use an afterloader to put a
10:38:56 radiation source in, you would do a dosimetry
10:38:59 calculation beforehand; correct?
10:39:00 A Yes.
10:39:02 Q There would be no reason to put a radiation
10:39:04 source into a patient without doing a dosimetry
10:39:06 calculation?
10:39:07 A No.
10:39:08 Q And that's been true for decades as well?
10:39:11 A Yes.
10:39:12 Q And that's true whether it's an afterloader or

Page 50

11:11:43 prescription dose at a depth, let's say, 1 centimeter or
11:11:48 2 centimeters, what would the surface dose be for each
11:11:52 of these three distributions of radioactive sources. So
11:11:58 for C, it's other than it is for B, which is lower than
11:12:02 it is for A.
11:12:05 Q And then each of these lines on Figure 7-D
11:12:10 approach the dotted line 52.
11:12:13 Do you understand what the dotted line 52 is
11:12:17 supposed to represent on this graph?
11:12:19 A That's the prescription dose at a depth, I
11:12:22 believe in this situation, of 2 centimeters from the
11:12:35 wall of the surgical cavity.
11:12:37 Q Why is the profile of B different than the
11:12:45 profile of A?
11:12:51 A Because all of the radiation is further from
11:12:53 the wall of the cavity than it is in A.
11:12:57 Q And that's something a person of ordinary skill
11:13:05 in the art would have understood in 1997?
11:13:05 A Yes.
11:13:07 Q Is that the same reason that the profile of C
11:13:10 is different from A?
11:13:11 A Yes.
11:13:12 Q Why is the profile of C different from the
11:13:17 profile of B?
11:13:20 A Because C is a point source, and, therefore,

Page 51

11:13:22 all of the radiation in that figure is further away from
11:13:28 the surgical wall, the wall of the surgical cavity.
11:13:38 Q Is it correct to say that the ratio of the dose
11:13:44 at the surface of the outer volume to the dose at the
11:13:50 prescription depth for A is greater than it is for B,
11:13:55 which is, in turn, greater than it is for C?
11:14:03 A Say that one more time.
11:14:04 Q Is it correct to say that the ratio of the dose
11:14:07 at the surface to the dose at the prescription depth is
11:14:11 greater for A than it is for B, which, in turn, is
11:14:16 greater than C?
11:14:18 A Yes.
11:14:25 Q Is it your understanding of the patent that one
11:14:27 of the claims of the inventors as to the invention is
11:14:30 reducing a device which reduces that ratio -- that is
11:14:33 reducing the ratio of the dose at the surface to the
11:14:36 dose at the prescription depth?
11:14:39 A I think I would say it somewhat differently.
11:14:42 Q How would you say it?
11:14:43 A It's a way of predetermining the dose at the
11:14:48 surface, the ratio of the dose to the surface to the
11:14:52 ratio at the depth of interest.
11:14:55 Q Why do you say predetermine?
11:14:57 A Because you can use different radiation source
11:15:02 distributions, as shown here, to give you different

Page 52

11:15:05 doses at the surface for a fixed dose at depth.
11:15:09 Q Do the inventors here describe which of these
11:15:13 dose profiles, A, B and C, if any, they prefer?
11:15:21 A I don't believe they do.
11:15:23 Q Are -- is it your understanding that the dose
11:15:26 profiles of A -- let me try it a different way.
11:15:32 Is it your understanding that the configuration
11:15:33 of the device shown in 7-A to the device shown in 7-B
11:15:40 and 7-C are all devices of the invention of the '204
11:15:43 patent?
11:15:45 A I believe that they are all considered to be
11:15:50 different applications of the same device.
11:15:55 Q Will you turn to -- in Exhibit 2 to column 6?
11:16:01 A Yes.
11:16:02 Q At line 3, there is a sentence that starts,
11:16:06 Figure 7-A illustrates an interstitial brachytherapy
11:16:12 apparatus (device A), such as those employed in the '582
11:16:21 patent.
11:16:22 Do you see where I am?
11:16:23 A Yes.
11:16:25 Q The '582 patent is a different patent than this
11:16:27 one; correct?
11:16:33 A Yes.
11:16:33 Q Then do you see down below that at line 6 of
11:16:35 column 6, the patent says, Figure 7-B illustrates an

Page 53

11:16:39 interstitial brachytherapy apparatus (device B) of the
11:16:45 invention?
11:16:47 Do you see that sentence?
11:16:48 A Yes.
11:16:49 Q And then if you go down further to column 6,
11:16:52 line 12, it says the same thing with respect to Figure
11:16:56 7-C being a device of the invention?
11:16:59 A Yes.
11:17:02 Q What the inventors here are saying is that 7-A
11:17:05 is a different invention of a different patent and B and
11:17:09 C are inventions of this patent; is that correct?
11:17:11 A That's what they are saying; correct.
11:17:16 Q And if you turn to Figure 1 of the patent, does
11:17:25 that figure correspond with the type of device that is
11:17:29 shown in Figure 7-B?
11:17:31 A Yes.
11:17:31 Q If you look at Figure 3, does that device
11:17:36 correspond to the type of device shown in Figure 7-C?
11:17:46 A Just a moment.
11:17:46 Q Sure.
11:18:11 A Yes.
11:18:11 Q So if we go back to Figure 7, Figure 7-A is the
11:18:21 invention of one of their prior patents and Figure 7-B
11:18:25 and 7-C are inventions of this patent?
11:18:28 A That's correct.

Page 54

11:18:29 Q And what they have -- one of the aspects of the
11:18:33 invention of this patent that the inventors have
11:18:36 highlighted as an advantage is the ability of the
11:18:39 configurations of 7-B and 7-C to reduce the dose at the
11:18:45 surface while still obtaining the same dose at the
11:18:48 prescription depth as compared to 7-A?
11:18:51 A That's correct.
11:18:52 Q And A person of ordinary skill in the art,
11:18:59 looking at these diagrams, the schematic diagrams 7-A,
11:19:04 7-B and 7-C, would understand the profiles to be as they
11:19:09 are shown in 7-D?
11:19:11 A Yes.
11:19:11 MR. SU: Object to the form.
11:19:12 BY MR. MAURER:
11:19:12 Q They would not have to do any calculations for
11:19:15 it?
11:19:15 A Correct.
11:19:20 Q Does the patent describe what the -- does the
11:19:24 patent put any numbers on the ability of devices B or C
11:19:31 to reduce the dose at the surface as compared to A?
11:19:45 A One moment.
11:19:46 Q Actually, I can point you to a section and you
11:19:49 can confirm whether this is true or not.
11:19:51 Column 6, right around the paragraph starting
11:19:57 line 42, 43 --

Page 55

11:19:59 A Yes.
11:20:11 MR. SU: Can I have that question again,
11:20:12 please?
11:21:08 THE WITNESS: Let me have your question again.
11:21:09 BY MR. MAURER:
11:21:10 Q Let me break it down for you, Doctor.
11:21:13 If you look at column 6 in that section we
11:21:18 talked about, around line 45, the authors give what they
11:21:20 calculate to be the dose for a 4-centimeter diameter
11:21:25 device of the type A; is that right?
11:21:29 A Yes.
11:21:29 Q And what is that dose?
11:21:32 A They say 131 Gray.
11:21:34 Q And that's at the surface?
11:21:37 A At the surface.
11:21:39 Q If you look to column 7, at line 6 -- starting
11:21:48 at line 6, do the authors give a dose for that same
11:21:51 4-centimeter diameter outer balloon for the
11:21:55 configuration of device C?
11:21:57 A Yes.
11:21:58 Q And what is that?
11:21:59 A 94 Gray.
11:22:02 Q And the inventors say that this decrease from
11:22:06 131 Gray to 94 Gray is a significant decrease; is that
11:22:11 correct?

Page 56

11:22:12 A That's correct.
11:22:23 Q What is the ratio of the surface for
11:22:26 configuration A for the surface dose to the prescription
11:22:30 dose based on those numbers?
11:22:34 A Based on those numbers, it would be 131 to 52.
11:22:40 Q I'm sorry. 52, I think, is just the patent's
11:22:45 way of referring to that line.
11:22:46 If you look at column 7, at line 10, I think
11:22:50 they give the dose.
11:22:51 A I see 60 Gray. So 131 divided by 60.
11:23:02 Q That's divided by two?
11:23:04 A Yes.
11:23:04 Q That's the ratio of the dose at the surface to
11:23:09 the dose at the prescription depth for configuration A;
11:23:16 correct?
11:23:16 A Yes.
11:23:18 Q What is the ratio of the dose at the surface to
11:23:21 the prescription dose for configuration C?
11:23:26 A Ratio would be 94 to 60.
11:23:29 Q A little more than one and a half?
11:23:31 A Right.
11:23:39 Q Will you turn back a page to column 6, line 61
11:23:44 to 62. It starts, Comparing the plots A, B and C, the
11:23:53 absorbed dose profile...
11:23:55 Do you see where I am?

Page 57

11:23:56 A M-hm.
11:23:57 Q What is meant -- how would a person of ordinary
11:24:01 skill in the art understand "absorbed dose profile"?
11:24:07 A It's the same as dose distribution, but they
11:24:11 are showing it in a two-dimensional form.
11:24:14 Q This would be the dose profile from the outer
11:24:16 surface of the balloon to the prescription depth?
11:24:21 A Correct.
11:24:32 Q Is it true that the inventors in this patent
11:24:36 claim that one of the advantages of the ability of
11:24:39 configurations B and C to control the dose at the
11:24:45 surface of the device is that it reduces the risk of
11:24:49 healthy tissue necrosis?
11:24:56 A Yes.
11:24:56 Q And that's something that a person of ordinary
11:24:59 skill in the art would understand based on looking at
11:25:04 Figures 7-A through 7-D; right?
11:25:08 A M-hm.
11:25:09 MR. SU: Object to form.
11:25:10 BY MR. MAURER:
11:25:10 Q Is that a yes?
11:25:12 A Yes. Sorry.
11:25:13 Q That's because a person of ordinary skill in
11:25:16 the art would understand that reducing the dose reduces
11:25:20 the risk of necrosis?

Page 58

11:25:21 A Yes.
11:25:25 Q Let me hand you another blank sheet of paper, which I need to find since I've written on the top, which I'll mark as Exhibit 5. Actually, rather than blank, I'm going to draw on this one for you.
11:25:41 (Plaintiff's Exhibit 5 was marked for identification by the Court Reporter.)
11:25:41 BY MR. MAURER:
11:25:46 Q How did you annotate the outer volume of Figure 7 in Exhibit 2 of the patent? If you look at Figure 7 --
11:25:54 A O.V.
11:25:55 Q I've handed you Exhibit 5 and I have drawn on there an outer circle, which I've denoted OV for outer volume, just like in Figure 7, and then an inner circle, which I intend to be a inner balloon filled with a radioactive liquid, sort of like it is in Figure 7 B.
11:26:10 Do you understand what I've shown there?
11:26:13 A Yes.
11:26:34 Q Can you please draw the radiation isodose profile for that inner balloon?
11:26:37 A Are you asking me to draw the dose as a function of distance from the wall of the outer volume?
11:26:43 Q That's a good point. Let's start by drawing the isodose curves around that -- the inner balloon.
11:26:52

Page 59

11:26:57 A Okay. They would, obviously, be concentric spheres.
11:27:10 Q Since we now have overlapping circles, can you label one or both of those as the side of a dose curve.
11:27:11 I initially asked you, Doctor, if you would draw the radiation isodose profile with respect to that inner balloon, and you asked me do I want you to do that with respect to the outer balloon. Do you remember that?
11:27:13 A Yes.
11:27:27 Q Yes, I do. Can you do that?
11:27:29 A You have to tell me at what point I need to give it to you.
11:27:34 Q Why is that?
11:27:37 A Well, because, obviously, if we're very close to the inner balloon, the dose will be higher, and the dose will be falling off closer to 1 over R than for a point on the opposite side of the outer volume where the dose will be less and be falling off closer to 1 over R squared.
11:27:41 Q And what you just described, the difference in dose profile depending on where you are with respect to that outer volume, that would have been understood by a person of ordinary skill in the art in 1997?
11:27:42 A Oh, yes.
11:27:42
11:27:44
11:27:46
11:27:48
11:27:50
11:27:52
11:27:57
11:28:02
11:28:07
11:28:16
11:28:16
11:28:16
11:28:19
11:28:22
11:28:25

Page 60

11:28:26 Q Well before that as well?
11:28:27 A Yes.
11:28:40 Q In your practice or in your experience, have you become familiar with the dose that is used to treat tumors that are located within the brain?
11:28:43
11:28:48
11:28:52 A Yes.
11:28:53 Q And what is the standard dose for treating tumors in the brain?
11:28:57
11:28:58 MR. SU: Objection, form.
11:29:06 THE WITNESS: I could give you an answer to that, but it depends on a very large number of things.
11:29:07
11:29:10 BY MR. MAURER:
11:29:11 Q Okay. Please do; then you can tell me what it depends on.
11:29:15 A Yes, it depends on the number of doses or the number of fractions that you're giving. It depends on the volume of tissue to be eradiated. It depends on the number of -- the length of the radiation course, whether it's one treatment per day or multiple treatments per day.
11:29:16
11:29:21
11:29:24
11:29:31
11:29:34
11:29:37
11:29:40 The standard answer would be approximately 60 Gray given at a conventional 2 Gray per day dose rate, an external radiation source.
11:29:45
11:29:52
11:29:58 Q And is that whole brain radiation or partial brain radiation?
11:30:01

Page 61

11:30:02 A No, that's partial brain.
11:30:10 Q And when you say give when an external radiation source, what sort of source or sources are we talking about?
11:30:12
11:30:15
11:30:16 A Linear accelerator X-ray beams.
11:30:20 Q Is there a name for that type of treatment?
11:30:25 A External X-ray.
11:30:28 Q External beam radiation therapy?
11:30:31 A External beam radiation therapy, exactly.
11:30:34 Q What is 3D conformal radiation therapy?
11:30:42 A 3D conformal therapy simply means that you're treating a local area in the patient with multiple beam directions, each one of which is shaped appropriately for the projected shape of the target from that direction.
11:30:47
11:30:53
11:31:00
11:31:04
11:31:10 Q Are you familiar with -- let me ask you a follow-up question on that.
11:31:14 Is 3D conformal therapy an external beam therapy?
11:31:15
11:31:19 A Yes.
11:31:20 Q What is IMRT?
11:31:21 A IMRT is the next advancement beyond 3D conformal radio therapy. And it allows you to not only shape each beam in two dimensions according to the projection from that direction, but to change the
11:31:25
11:31:32
11:31:38
11:31:42

Page 62

11:31:50 1 intensity of the dose across that shape in such a way
11:31:52 2 that the final dose distribution is more conformal to
11:31:58 3 the three-dimensional shape of the target than you could
11:32:01 4 do with multiple two-dimensionally-shaped beams.
11:32:07 5 Q When did IMRT become available?
11:32:11 6 A Mid 1990s in some places.
11:32:17 7 Q What about in the U.S.?
11:32:19 8 A We had it in 1995.
11:32:22 9 Q What about in the U.K.?
11:32:26 10 A Later.
11:32:28 11 Q What about -- when did 3D conformal radiation
11:32:32 12 therapy become available in the U.K.?
11:32:36 13 A I'm not sure I can answer for the U.K. in that
11:32:39 14 case.
11:32:40 15 Q What about in the U.S.?
11:32:42 16 A In the U.S., '89, '90.
11:32:50 17 Q And prior to 3D conformal radiation, what was
11:32:54 18 the type of radiation that was given?
11:32:57 19 A We would call it conventional 2D therapy these
11:33:01 20 days.
11:33:02 21 Q And what is that?
11:33:04 22 A It means that the patient would -- the patient
11:33:10 23 treatment plan would be designed on the basis of
11:33:14 24 projection X-rays taken of a patient from particular
11:33:20 25 directions in a process called simulation.

Page 63

11:33:25 1 Typically, the number of beams would be small,
11:33:30 2 two or three, sometimes four, and the patient -- the
11:33:37 3 source of information that you do the treatment plan is
11:33:41 4 two-dimensional as opposed to three-dimensional CT. So
11:33:44 5 you would not have density information; you would only
11:33:48 6 have projected two-dimensional anatomical information.
11:33:54 7 Q What was the effect of having a smaller number
11:33:58 8 of beams for conventional 2D therapy as compared to the
11:34:01 9 3D conformal or IMRT therapies?
11:34:05 10 A It would be a poorer confirmation of the dose
11:34:11 11 to the shape of the volume and generally higher doses to
11:34:16 12 neighboring tissues.
11:34:19 13 Q What percentage of the brain would be eradiated
11:34:22 14 in a conventional 2D therapy treatment?
11:34:29 15 A There really -- you have not given me enough
11:34:31 16 information to answer that question, I think.
11:34:33 17 Q What more would you need?
11:34:35 18 A I would need to know the size of volume you're
11:34:39 19 attempting to radiate as an example.
11:34:41 20 Q Fair enough. Let's say a 2-centimeter diameter
11:34:44 21 tumor.
11:34:48 22 A Another piece of information I would need is
11:34:52 23 what percentage of the prescription dose are you asking
11:34:57 24 about? In other words, if you asked about what
11:35:01 25 percentage would get 50 percent of the prescription

Page 64

11:35:04 1 dose, the answer is different than what percentage would
11:35:08 2 get 10 percent of the prescription dose.
11:35:08 3 Q Fair enough. Why don't we say 100 percent of
11:35:13 4 the dose?
11:35:13 5 A 100 percent of the dose would typically be a
11:35:19 6 volume which is fairly close to the volume of the
11:35:23 7 target, maybe 10 to 20 percent larger than the dose --
11:35:30 8 than the target volume itself.
11:35:31 9 Q Would any of the tissue in the brain receive
11:35:33 10 more than 100 percent of the dose?
11:35:35 11 A Normally only tissues inside the target would
11:35:41 12 be receiving doses of higher than 100 percent, although
11:35:44 13 that is not a universal statement.
11:35:50 14 Q Why isn't it a universal statement, Doctor?
11:35:53 15 A Again, we have to know the number of beams that
11:35:55 16 are being used.
11:35:56 17 So if you were just using two beams, if the
11:36:01 18 energy was low, then there could be point in a normal
11:36:03 19 brain that would get higher doses than the dose at
11:36:08 20 target.
11:36:14 21 Q I believe you gave me a range of two to three
11:36:17 22 beams and sometimes four; is that correct?
11:36:19 23 A Yes.
11:36:20 24 Q Can you give me a breakdown as to how many were
11:36:22 25 two, how many were three, and how many were four in the,

Page 65

11:36:25 1 I guess, late '80s, early '90s?
11:36:30 2 A What country? What time period?
11:36:33 3 Q Well, the time period is, let's say, 1990 in
11:36:37 4 the U.S.
11:36:45 5 A I would guess maybe 50 percent of the
11:36:53 6 treatments would be two fields, 50 percent would be
11:36:56 7 three fields.
11:36:57 8 Q How about in the U.K.?
11:36:58 9 A Less.
11:37:01 10 Q Less which way?
11:37:03 11 A They would sometimes use single fields or
11:37:07 12 two-field maximum. Rarely use more than two in those
11:37:12 13 days.
11:37:12 14 Q Is it fair to say the U.K. lagged behind the
11:37:15 15 U.S. in external beam radiation therapy?
11:37:19 16 A I think that's correct.
11:37:20 17 Q Why is that?
11:37:24 18 A Are you talking about politics?
11:37:26 19 Q Well, is there a scientific reason or is it a
11:37:30 20 political reason or just generally?
11:37:32 21 A I would say politics.
11:37:37 22 Q And you would have to do a specialized
11:37:39 23 medicine?
11:37:39 24 A In my opinion, yes.
11:37:42 25 Q You don't need to go any further.

balloon.

When the device of Ashpole is inserted into the patient, is the balloon inflated prior to its insertion?

A No.

Q It's at some time after it's placed in the patient that the balloon is inflated; correct?

A Correct.

Q And do you agree that there comes a point when the balloon is inserted into the patient, and after the outer -- I'm sorry -- the outer surface has been expanded, that radioactive spheres are placed inside of the catheter at the far end, inside of the area surrounded by the balloon?

A Yes, that's described.

Q Of the figures in the '204 patent that we looked at, Figure 7-A, B, and C, which of those is the Ashpole closest to in its physical configuration?

MR. SU: Objection, form.

BY MR. MAURER:

Q 7-A, B and C is what I'm referring to.

A Yes. I would have to say 7-C, those three choices.

Q Dr. Verhey, you said of those three, you would have to say it's 7-C.

How is the configuration of the Ashpole device

different from the device of 7-C, if at all?

A Because he describes the use of multiple sources in a line as opposed to an individual source at the center.

Q The sources that Ashpole describes, are they spherical sources?

A I believe they are -- they are beads.

Q And how many beads does Ashpole discuss using in his device?

A About a dozen active sources, is what it says.

Q For a typical case?

A For a typical case.

Q Given the dose rate and dose that Dr. Ashpole discusses in his patent that he is attempting to achieve, and knowing that the radionuclide in this case is Caesium-137, could a person of ordinary skill in the art calculate how many active sources are needed for a particular balloon configuration?

MR. SU: Objection, form.

THE WITNESS: You could calculate that only if you know the dimensions and shape of the surgical cavity.

BY MR. MAURER:

Q For a particular balloon configuration, knowing the dose and dose rate that Dr. Ashpole hopes to

achieve, could a person of ordinary skill in the art calculate the dose at the surface of that balloon and -- let me try that again.

Given a particular -- the particular dose that Dr. Ashpole describes in his article and dose rate, could a person of ordinary skill in the art calculate how many sources of Caesium-137 are needed to achieve that dose at the surface of a balloon for a particular configuration of the balloon, a particular size of the balloon?

A If you knew the activity of the sources.

Q Does Caesium-137 have a known activity?

A No. It can be obtained in different activities, different activity levels.

Q If you look at page 334 of Ashpole, Exhibit Number 6, under apparatus --

A Yes.

Q -- the second paragraph, does it discuss the activity of the beads?

A It does. It says they have a nominal activity of 1.4 giga becquerels each.

Q In paragraph 14 of your declaration, Exhibit 1, you start to discuss how the Ashpole device is used. I want to go through that with you, if we may.

You agree that the Ashpole device is used after

resection of a brain tumor?

A Yes.

Q And the Ashpole device is inserted during the same procedure during which the brain tumor has been resected?

A Yes.

Q What would a person of ordinary skill in the art understand about the physical consistency of brain tissue? Is it hard? Is it soft? Is it spongy? How would a person of ordinary skill in the art describe it?

A I would say that's a better question for a neurosurgeon than a physicist.

Q Can you answer the question as a physicist?

A I think spongy is the best word of those three that you just gave me.

Q Is there a better word you can think of?

A No. It's not hard.

Q When a tumor is located in brain tissue, is there pressure on the surrounding brain tissue?

A It often can, because there is fluid produced by the tumor cells which can create pressure on the neighboring cells.

Q And, in fact, doesn't the mass of the tumor itself lead to some pressure on the brain tissue?

A It very well can.

Page 74

11:55:52 Q Some of the symptoms that come from having
11:55:55 brain cancer are due to the mass effects of the tumor;
11:56:00 is that correct?
11:56:00 A Yes, that's correct.
11:56:02 Q So it's something a person of ordinary skill in
11:56:06 the art would know?
11:56:12 A I'm not sure I know the answer to that
11:56:14 question.
11:56:16 Q The person of ordinary skill in the art is one
11:56:19 that you've defined as being or having the
11:56:21 qualifications to be board certified.
11:56:24 Would that person know that the tumor in a
11:56:30 brain can cause pressure effects due to its mass?
11:56:34 A I think I would expect that person to know,
11:56:38 yes.
11:56:44 Q In the Ashpole device -- I'm sorry, not the
11:56:47 Ashpole. Let me state in general here.
11:56:50 When a neurosurgeon resects the tumor, what
11:56:53 they are doing is surgically removing the cancerous
11:56:58 cells; is that correct?
11:56:59 A Correct.
11:57:01 Q Do they remove any margin of healthy brain with
11:57:04 the cancer cells?
11:57:06 MR. SU: Objection, form.
11:57:07 THE WITNESS: That's certainly a question I

Page 75

11:57:09 should not answer.
11:57:10 BY MR. MAURER:
11:57:12 Q Why shouldn't you answer it?
11:57:14 A Because I'm not expected as a person of
11:57:16 ordinary skill in the art to know the answer to that
11:57:19 question.
11:57:21 Q Not speaking from a person of ordinary skill in
11:57:24 the art perspective, from your own personal knowledge,
11:57:28 Dr. Verhey, does a neurosurgeon remove any portion of
11:57:31 healthy brain when they resect a tumor?
11:57:34 A Often they do, yes.
11:57:37 Q Why do they do so?
11:57:43 A Because the more tumor cells that can be
11:57:45 removed, then the assumption is that the region just
11:57:50 outside the tumor probably has a low concentration of
11:57:57 tumor cells in it. The lower the tumor burden remaining
11:57:59 in the patient, the likelier that radiation, as an
11:58:03 example, will kill off the remaining cells.
11:58:10 Q If a tumor is in the brain, it seems obvious
11:58:15 that the physician physically has to get to the tumor in
11:58:19 order to resect it; correct?
11:58:21 A Yes.
11:58:21 Q And in order to do so, the physician will
11:58:24 manipulate and move surrounding brain tissue to get to
11:58:28 the cancer cells?

Page 76

11:58:29 A Yes.
11:58:32 Q And in doing that manipulation, the physician
11:58:36 will to some extent compress the surrounding brain
11:58:40 tissue?
11:58:42 MR. SU: Objection, form.
11:58:48 THE WITNESS: I would say very likely.
11:58:50 BY MR. MAURER:
11:58:50 Q Some compression of brain tissue is allowable,
11:58:54 it's just problems develop if brain tissue is overly
11:59:01 compressed; is that fair?
11:59:04 A Yes.
11:59:04 Q When a tumor is removed from the brain, what is
11:59:08 the shape of the cavity?
11:59:16 A It varies from patient to patient.
11:59:18 Q It depends on the shape of the tumor?
11:59:20 A Yes.
11:59:20 Q Does it depend on what type of tumor it is?
11:59:22 A No, I would not think it's strongly correlated
11:59:25 to that.
11:59:26 Q Do gliomas have different shapes from
11:59:29 metastasis?
11:59:33 A Metastasis are more likely to be spherical than
11:59:37 gliomas.
11:59:38 Q What shape are gliomas likely to be?
11:59:42 A Any shape.

Page 77

11:59:45 Q In the Ashpole article, what does he
11:59:47 describe -- what type of tumor does he describe
11:59:52 treating?
11:59:52 A He talks about treating gliomas.
12:00:09 Q When a tumor is resected, would a person of
12:00:14 ordinary skill in the art expect a cavity to have smooth
12:00:18 walls or would they expect the walls to be -- have
12:00:21 crooks and -- nooks and crannies?
12:00:32 MR. SU: Objection, form.
12:00:33 THE WITNESS: Again, I would say that that is
12:00:35 not a question that a person of ordinary skill in the
12:00:37 art, as I have defined it, would be expected to know.
12:00:43 BY MR. MAURER:
12:00:44 Q Sitting here in your personal capacity, do you
12:00:46 know?
12:00:46 A Yes, certainly, they have nooks and crannies.
12:00:58 Q In the case of a tumor that is through its mass
12:01:02 creating pressure in the brain tissue, when the tumor is
12:01:08 resected, what happens to the space, the cavity where it
12:01:12 was?
12:01:15 A It tends to fill with fluid and the tissues
12:01:22 tend to move into the cavity over a period of time.
12:01:29 Q Another way of saying that is that the cavity
12:01:33 would tend to collapse around the resection site?
12:01:38 A Over a period of time, there would be some

Page 78

12:01:40 collapse.
12:01:41 Q How much?
12:01:42 A I don't know.
12:01:50 Q Over what period of time?
12:01:52 A Probably months.
12:01:56 Q Is that something you know or just something
12:01:58 you're saying?
12:02:01 MR. SU: Objection, form.
12:02:05 THE WITNESS: I've seen post-operative studies
12:02:07 of the brain which show a surgical cavity, which is
12:02:12 somewhat smaller than the cavity seen immediately after
12:02:15 the operation.
12:02:21 So a few month later when the patient is being
12:02:23 examined for possible recurrence, you will see the
12:02:27 remaining surgical cavity, and you could compare it to
12:02:30 what it looked like immediately after surgery.
12:02:32 BY MR. MAURER:
12:02:32 Q Does that mean there was no decompression of
12:02:37 the tissue or collapse of the tissue immediately after
12:02:40 surgery?
12:02:41 A I don't know.
12:02:44 Q Who would know that?
12:02:45 A Neurosurgeon.
12:02:48 Q What about a radiation oncologist?
12:02:51 A Very likely.

Page 79

12:03:01 Q So now let me go back to Ashpole.
12:03:03 First the tumor is resected, we said; right?
12:03:07 A Yes.
12:03:07 Q Then the balloon in an inflated state is
12:03:10 inserted into the cavity?
12:03:12 A Yes.
12:03:12 Q Then the balloon is inflated?
12:03:14 A Yes.
12:03:14 Q In paragraph 14 of Exhibit 1 -- this is the
12:03:17 sentence that spans pages 4 and 5 of your report -- you
12:03:22 say that the volume of fluid used varies according to
12:03:26 the size of the tumor bed.
12:03:30 Do you see where I am?
12:03:31 A Yes.
12:03:32 Q Why did you include that statement in your
12:03:34 report?
12:03:53 A Because it's so obvious. Is that the question?
12:03:56 Q Let me ask a different question.
12:03:59 Did you read Ashpole to mean that for larger
12:04:02 tumor beds he would use more fluid and for smaller tumor
12:04:07 beds he would use less fluid to fill the balloon?
12:04:11 A Yes.
12:04:18 Q What Ashpole teaches is for the physician to
12:04:22 configure the balloon to fill the tumor cavity by using
12:04:25 the amount of fluid required to do so?

Page 80

12:04:28 A It does not quite say that.
12:04:30 Q Let's take a look at it. What do you think it
12:04:33 says?
12:04:37 A I would like to find the exact words.
12:04:49 Q I believe you refer to page 334 at column 2 in
12:04:54 your report.
12:05:22 VIDEOGRAPHER: This is the end of videotape
12:05:23 number one. We are going off the video record. The
12:05:26 time is 12:05 p.m.
(Recess Taken.)
12:07:17 VIDEOGRAPHER: This is the beginning of
12:07:18 videotape number two. We are now back on the video
12:07:21 record. The time is 12:07 p.m.
12:07:23 MR. MAURER: Can I ask Madam Court Reporter, I
12:07:28 believe, to read the last two questions and answers that
12:07:28 are relevant?
(Record Read.)
12:08:02 THE WITNESS: Yes. The sentence says, The
12:08:05 modified catheter was then inserted under direct vision
12:08:09 so that the inflated balloon filled the post-surgical
12:08:12 cavity.
12:08:15 BY MR. MAURER:
12:08:16 Q So is it true, Dr. Verhey, that Dr. Ashpole
12:08:19 teaches the physician to configure the balloon to fill
12:08:22 the tumor cavity by using the amount of fluid required

Page 81

12:08:25 to do so?
12:08:27 A It does say that.
12:08:28 MR. SU: Objection, form.
12:08:29 BY MR. MAURER:
12:08:37 Q In this section that you just read, Dr. Ashpole
12:08:41 discusses the post-surgical cavity, that first part of
12:08:47 the right-hand column.
12:08:50 Do you see that?
12:08:51 A Yes.
12:08:52 Q And then in the next paragraph he discusses the
12:08:55 tumor bed.
12:08:56 Do you see that?
12:08:59 A Yes.
12:09:00 Q Is there a difference between those two
12:09:02 concepts, or would a person of ordinary skill in the art
12:09:05 understand them to be the same?
12:09:17 MR. SU: Objection to form.
12:09:20 THE WITNESS: He's not very explicit about
12:09:21 this, to tell you the truth, because when he says a
12:09:24 typical case needed 15 ML to give a balloon diameter of
12:09:29 2.9 centimeters, it implies to me that that is a
12:09:34 spherical balloon. And given the fact that the surgical
12:09:41 cavity is unlikely to be spherical, there is a question
12:09:47 about how well it -- the spherical balloon can fit
12:09:52 inside a nonspherical cavity, in my mind.

Page 82

12:09:56 BY MR. MAURER:
12:09:59 Q My question was a different one.
12:10:01 My question was, Dr. Ashpole uses the phrase
12:10:04 "surgical cavity," and he also uses the phrase "tumor
12:10:11 bed." And is he talking about the same thing or is he
12:10:15 talking about something different with those two
12:10:17 phrases?
12:10:17 A I'm sorry. I did not answer your question.
12:10:21 No, I think they are the same thing.
12:10:28 Q And after --
12:10:35 MR. MAURER: Take a short break here.
12:10:57 VIDEOGRAPHER: We are going off the record.
12:10:57 The time is 12:10 p.m.
(Lunch Recess Taken.)

Page 83

AFTERNOON SESSION
01:19:24 VIDEOGRAPHER: We are now back on the video
01:19:26 record. The time is 1:19 p.m.
01:19:28 BY MR. MAURER:
01:19:29 Q Dr. Verhey, before we were interrupted by the
01:19:31 fire alarm and decided to take our lunch, we were
01:19:35 talking about the Ashpole article. I'll ask you to pull
01:19:39 that out again. It's Exhibit 6.
01:19:51 A Yes.
01:19:52 Q And if you also pull out your declaration,
01:19:53 Exhibit 1.
01:19:54 We discussed before lunch that the balloon in
01:19:58 Ashpole is filled with fluid after the device is
01:20:02 inserted into the cavity. Do you recall that?
01:20:04 A Yes.
01:20:04 Q Once the fluid is inserted, you agree that it's
01:20:07 not removed again until the treatment is completed?
01:20:11 A That's right.
01:20:14 Q In paragraph 14 of your report, you state that
01:20:21 this fluid is -- I'm at the bottom of page 4 -- quote, a
01:20:28 radio-opaque fluid, open parentheses, needed for
01:20:32 treatment planning purposes, close parens.
01:20:35 Do you see that?
01:20:35 A M-hm.
01:20:37 Q Why is a radio-opaque fluid needed for

Page 84

01:20:40 treatment planning purposes?
01:20:42 A Because then on an X-ray taken before
01:20:45 treatment, you can see the diameter of the flu balloon
01:20:51 that you'll fill with sources -- that you'll put the
01:20:54 sources in.
01:20:55 Q The radio-opaque fluid allows you to see the
01:20:59 balloon in the cavity; correct?
01:21:01 A Right.
01:21:02 Q And Ashpole actually addresses the reason for
01:21:07 the radio-opaque fluid on page 334, the right-hand
01:21:13 column, the first full paragraph --
01:21:17 A M-hm.
01:21:18 Q Dr. Ashpole says that the balloon was filled
01:21:20 with the contrast fluid, quote, to facilitate later
01:21:25 X-ray visualization and dosimetry calculations?
01:21:30 A Right.
01:21:33 Q And the X-ray visualization Dr. Ashpole is
01:21:36 talking about there is the X-ray visualization of the
01:21:41 balloon in the cavity; correct?
01:21:43 A Yes.
01:21:45 Q And the dosimetry calculations is the dose
01:21:48 that's to be delivered to the tissue surrounding that
01:21:52 balloon and cavity?
01:21:57 A That would be ideal.
01:22:05 Q And, in fact, if you turn to page 335, which is

Page 85

01:22:10 the next page of Ashpole, he discusses under the section
01:22:16 Dosimetry Calculation how he goes about that dosimetry
01:22:20 calculation; is that correct?
01:22:21 A Yes.
01:22:22 Q And in Figure 3, there is a picture.
01:22:27 What is the picture in Figure 3 of?
01:22:30 A The picture is a figure -- this figure is a
01:22:32 picture of the dose distribution around the radio-opaque
01:22:41 balloon.
01:22:42 Q This is -- sorry.
01:22:43 A I'm sorry. The balloon filled with
01:22:45 radio-opaque solution.
01:22:47 Q This radiograph that's in Figure 3 is of the
01:22:51 type that he's discussing that would have been taken to
01:22:56 facilitate the X-ray visualization and the dosimetry
01:23:00 calculation and this actually has a dosimetry
01:23:02 calculation on it?
01:23:04 A Yes, that's right.
01:23:13 Q The picture of Figure 3 has some crosses
01:23:17 depicted in the balloon.
01:23:19 Do you see that?
01:23:20 A Yes.
01:23:20 Q What are those crosses?
01:23:23 A I believe those are the locations of the dummy
01:23:28 source, the dummy source train.

Page 86

01:23:31 Q What is a dummy source train?
01:23:33 A It's a wire with small beads attached that are
01:23:39 not radioactive but that mimic the actual radioactive
01:23:43 train that will be used for the treatment.
01:23:46 Q Why is a dummy source train used?
01:23:49 A Because then you can look at that source train
01:23:52 and determine a dose calculation based on several
01:23:57 assumptions about where the radioactive sources would be
01:24:00 in the real source train.
01:24:05 Q There's also some rings drawn in that surround
01:24:11 the balloon.
01:24:12 Do you see that?
01:24:12 A Yes.
01:24:13 Q What are those rings?
01:24:14 A Those are dose profiles, dose surface,
01:24:20 actually.
01:24:22 Q You say dose surfaces because they are 3D?
01:24:25 A Yes, they would be 3D, although you're seeing
01:24:27 them in 2D.
01:24:29 Q Those dose surfaces were calculated based on
01:24:32 the dummy source train?
01:24:34 A Based on their assignment of where the
01:24:37 radioactive sources will be relative to that as dummy
01:24:42 sources, yes.
01:24:45 Q In your Exhibit 6, in Figure 1, can you outline

Page 87

01:24:50 in orange where the cavity is? I've given you an orange
01:24:55 highlighter.
01:25:00 A Well, no, actually, I can't.
01:25:02 Q Why not?
01:25:03 A Because the only thing you can see is the
01:25:05 radio-opaque filled balloon; you can't actually see
01:25:09 where the surface of the cavity is.
01:25:11 Q What is that that is surrounding the
01:25:13 radio-opaque balloon that's in a darker color?
01:25:17 A Tissue.
01:25:19 Q And doesn't the tissue define the cavity?
01:25:24 A It might, but not necessarily in three
01:25:26 dimensions. I don't know actual exactly where the
01:25:30 tissue cavity is, where all the cavity is. All I can
01:25:35 see is the balloon for sure.
01:25:36 Q Based on this 2D slice that you see, can you
01:25:42 outline where the cavity is?
01:25:42 A It would be very close to the line that's
01:25:42 designated 200.
01:25:44 Q Can you do that in orange, please?
01:25:50 MR. SU: Object to the form.
01:25:52 THE WITNESS: It's a very big marker, yes.
01:25:54 BY MR. MAURER:
01:25:55 Q Can you use the point of it -- or here's a red
01:25:57 pen. How about you try that instead.

Page 88

01:26:18 Can I actually see the exhibit so -- you can
01:26:21 keep the pen if you want. It's Howrey's pen.
01:26:29 Could you in this figure for me in blue outline
01:26:34 the balloon surface? I have a blue pen if you need one.
01:26:44 A Given the thickness of the various markers,
01:26:46 there is no way I can differentiate between the balloon
01:26:50 surface and the cavity.
01:27:01 Q When you say the thickness of the different
01:27:03 markers, you mean the pens? What do you mean by
01:27:05 markers?
01:27:06 A Yes, the pens.
01:27:08 Q In Figure 3 at least, the cavity conforms to
01:27:13 the balloon? You agree with that?
01:27:15 MR. SU: Objection, form.
01:27:18 THE WITNESS: I cannot see any differentiation
01:27:20 between the balloon and the cavity in this figure.
01:27:22 BY MR. MAURER:
01:27:29 Q Do you agree that the dose distributions shown
01:27:32 in Figure 3 are substantially similar in shape to the
01:27:34 balloon shown in Figure 3?
01:27:37 A Yes.
01:27:44 Q If you look to your report, in paragraph 16,
01:27:57 the second sentence starts, Ashpole produces a desired
01:28:01 mean dose rate at a given distance from the balloon
01:28:04 surface...

Page 89

01:28:04 Do you see that?
01:28:05 A Yes.
01:28:06 Q What is that distance?
01:28:16 A It depends on the prescription.
01:28:18 Q What does Ashpole say that distance is?
01:28:21 A I think there was one example where he talks
01:28:25 about it being -- I believe he talks about it being 5
01:28:29 millimeters. Let me check on that.
01:28:37 Q Sure.
01:28:40 A Yes, a distance of .5 centimeters in the blue
01:28:43 surface.
01:28:46 Q And it's not just a desired mean dose rate that
01:28:49 Ashpole produces at that distance; there is a -- he
01:28:54 produces a dose at that distance as well; correct?
01:28:59 A Once he tells us how long it will be there,
01:29:02 yes.
01:29:05 Q What is the dose that he produces at .5
01:29:10 centimeters for the balloon surface?
01:29:13 A 50 Gray.
01:29:15 Q And he says that that is the total dosage that
01:29:18 is given to the tumor bed; correct?
01:29:20 A That's what he says, yes.
01:29:32 Q So Ashpole is defining the -- this volume, .5
01:29:38 centimeters, from the balloon surface as the tumor bed
01:29:41 in his article?

Page 90

01:29:44 A Yes, he is.
01:29:48 Q So what Ashpole is actually doing is
01:29:55 determining a dose with respect to the balloon surface
01:29:58 and using that as a proxy for the dose to the target
01:30:02 tissue; correct?
01:30:05 A That's correct. I think the only hedging that
01:30:09 he does is to use the word "about."
01:30:16 Q And the "about" is found in the dosimetry
01:30:18 calculation section?
01:30:19 A It says a dose rate of about 250 centigrade per
01:30:22 hour at a distance of a half-centimeter from the blue
01:30:26 surface, for a total dose of -- about 20 hours to give a
01:30:29 total dosage of 50 Gray to the tumor bed.
01:30:45 Q If you look to page 336, at the bottom
01:30:49 left-hand portion of the left column, he actually
01:30:57 describes the dose delivered as 50 Gray at .5
01:31:01 centimeters depth from the surface of the blue; is that
01:31:03 correct?
01:31:04 A That's correct.
01:31:13 Q The fact that Dr. Ashpole is determining the
01:31:15 dose with respect to the balloon as a proxy for the dose
01:31:19 to the tissue means that the balloon in the tissue are
01:31:22 in conformance with each other; correct?
01:31:25 MR. SU: Objection, form.
01:31:29 THE WITNESS: I believe he's hoping that they

Page 91

01:31:30 are, yes.
01:31:31 BY MR. MAURER:
01:31:57 Q Let me go back in your report to paragraph 15.
01:32:01 That's Exhibit 1.
01:32:04 A M-hm.
01:32:06 Q Are you there?
01:32:07 A Yes.
01:32:10 Q You start off paragraph 15 by saying, There is
01:32:12 no teaching in Ashpole that the balloon can be expanded
01:32:15 to conform the shape of the cavity to the outer surface
01:32:19 of the balloon; is that right?
01:32:21 A That's right.
01:32:22 Q And when you say that the balloon can be
01:32:25 expanded to conform the shape of the cavity to the outer
01:32:29 surface of the balloon, when are you talking about?
01:32:34 A Excuse me. When --
01:32:35 Q Is it -- there is no teaching to expand the
01:32:39 balloon once it's been implanted and initially expanded?
01:32:44 A That's correct.
01:32:51 Q Does the resected cavity of the gliomas of the
01:32:57 type that Ashpole is discussing in his article match the
01:33:03 spherical shape of a balloon?
01:33:07 A It seems unlikely that they would -- a person
01:33:14 of ordinary skill in the order would not expect those to
01:33:19 match. I wouldn't think so.

Page 92

01:33:30 Q Leaving aside the question of expansion, do you
01:33:33 agree that in Ashpole the cavity that is shown in Figure
01:33:36 1 does conform to the surface of the balloon?
01:33:41 A I would say that Ashpole is assuming that it
01:33:43 does in this paper.
01:33:45 Q And in Figure 1, it shows that the cavity shown
01:33:52 does conform with the balloon?
01:33:52 A It appears to do so, yes.
01:33:54 Q And do you agree that so long as the cavity
01:33:57 conforms to a balloon, a controlled dose can be
01:34:02 calculated and administered to the tissue surrounding
01:34:05 the balloon?
01:34:06 A Yes.
01:34:16 Q Why do you have the statement in your report
01:34:18 that there is no teaching that the balloon can be
01:34:20 expanded to conform the shape of the cavity to the outer
01:34:24 surface of the balloon?
01:34:25 A Because he does not say anywhere in here that
01:34:31 he does so.
01:34:33 Q Why do you point that out?
01:34:37 A Well, actually, it seemed odd to me, not that
01:34:41 it does not happen, but that he would assume that the
01:34:46 surgical cavity would be very closely aligned with the
01:34:50 sphere. And if he does not assume that, then he must be
01:34:55 assuming that the balloon shapes the cavity, but he

Page 93

01:35:02 never says it.
01:35:04 Q He does not say it, but a person of ordinary
01:35:07 skill in the art reading this paper and looking at
01:35:10 Figure 3 would see that the cavity does conform to the
01:35:15 shape of the balloon; correct?
01:35:18 MR. SU: Object to form.
01:35:21 THE WITNESS: They would see that in this
01:35:22 figure they appear to conform to each other, yes.
01:35:25 BY MR. MAURER:
01:35:26 Q And based on what a person of ordinary skill in
01:35:28 the art knows about the shapes of tumors and given what
01:35:33 they see in that figure and in this discussion, that a
01:35:36 person of ordinary skill in the art would assume that
01:35:40 the balloon has been shaped so as to conform the cavity
01:35:45 to the balloon, at least in part?
01:35:47 MR. SU: Objection, form.
01:35:50 THE WITNESS: They might wonder that, but I was
01:35:51 more struck by the fact that it was not described here.
01:35:55 I say -- there is no teaching. It does not say
01:35:58 blow the balloon up until it's in contact with the
01:36:02 surface. No matter what the shape of the cavity is, it
01:36:05 does not say that.
01:36:08 BY MR. MAURER:
01:36:08 Q It does say that the balloon is inserted and
01:36:11 expanded so as to fill the cavity?

Page 94

01:36:14 A Yes, it does.
01:36:15 Q Couldn't that be taken by a person of ordinary
01:36:17 skill in the art as a statement that the balloon is
01:36:19 expanded so that the cavity conforms to its surface?
01:36:24 A One might assume that, but I think it's odd
01:36:28 that -- as I say, that that is not pointed out here.
01:36:33 Q It's not explicitly stated in the paper, is
01:36:35 your observation?
01:36:40 A Right.
01:36:41 Q But a person of ordinary skill in the art
01:36:41 reading this could understand it that way?
01:36:44 MR. SU: Objection, form.
01:37:04 THE WITNESS: Yes, they could.
01:37:04 BY MR. MAURER:
01:37:05 Q You state further in paragraph 15 that there is
01:37:07 no teaching in Ashpole that the balloon comes into
01:37:10 contact with the tumor bed at all points?
01:37:14 A Correct.
01:37:23 Q Is that another way of stating what you said in
01:37:27 the first part of that sentence or is that a separate
01:37:30 point?
01:37:31 A I think it's sort of an emphasis to the earlier
01:37:34 point.
01:37:38 Q Does Claim 36 of the '204 patent require that
01:37:42 the balloon be expanded to conform the shape of the

Page 95

01:37:45 cavity to the outer surface of the balloon?
01:37:54 MR. SU: Objection, form, calls for a legal
01:37:56 conclusion.
01:38:21 THE WITNESS: I think I'll go along with Mr. Su
01:38:24 at this point and not answer that as currently stated
01:38:27 anyway.
01:38:27 BY MR. MAURER:
01:38:28 Q I'm sorry. You have not been instructed not to
01:38:31 answer, so it's your obligation to answer the question,
01:38:34 Doctor.
01:38:34 A Oh, okay.
01:38:41 MR. SU: If you can do so, but I have my
01:38:42 objection on the record.
01:39:17 THE WITNESS: No, it does not say that. In my
01:39:21 opinion, it says the apparatus provides a controlled
01:39:25 dose at the outer spacial volume expandable surface.
01:39:28 BY MR. MAURER:
01:39:31 Q Let's turn back to Exhibit 1. I want to go
01:39:40 back to paragraph 15 and look at the second sentence
01:39:43 now.
01:39:46 Do you see the second sentence?
01:39:48 A M-hm. Should I read it?
01:39:50 Q To yourself is fine.
01:39:52 A Yes.
01:39:59 Q You use the phrase "in their undue deformation

Page 96

01:40:02 and compression."
01:40:03 How much is undue?
01:40:06 A I think a neurosurgeon could answer that
01:40:08 question.
01:40:09 Q It's not something that a person of ordinary
01:40:12 skill in the art, as you've defined it, would be able to
01:40:15 answer?
01:40:15 A No.
01:40:15 Q Again, this is recognizing that some
01:40:18 compression is okay, some deformation is okay, it just
01:40:22 can't be undue; correct?
01:40:24 A Correct.
01:40:40 Q Let's turn back to Ashpole then. In particular
01:40:42 I want to go to the first page. It's always good to
01:40:47 begin at the beginning.
01:40:58 On the right-hand column, at the end of that,
01:41:02 Dr. Ashpole discusses some advantages of his new
01:41:05 technique of brachytherapy.
01:41:09 Do you see where I am?
01:41:10 A The last paragraph?
01:41:12 Q Yes.
01:41:13 A M-hm.
01:41:14 Q And one of the advantages that he discusses
01:41:18 there is the avoidance of salvage craniotomy for mass
01:41:23 effect caused by late radionecrosis as experienced in

Page 97

01:41:30 brachytherapy methods using wire implants.
01:41:34 Do you see that?
01:41:34 A Yes.
01:41:40 Q Let's break that down and try to understand as
01:41:43 a person of ordinary skill in the art would.
01:41:46 What is salvage craniotomy?
01:41:48 A It means when the patient experiences necrosis
01:41:52 following a radiation procedure, as an example, the
01:41:56 necrosis can and often is removed surgically. That
01:42:01 would be salvage craniotomy. You go in and remove the
01:42:08 carotid tissue surgically.
01:42:13 Q Craniotomy means surgery in the skull?
01:42:15 A Yes, open the cranium.
01:42:17 Q And late radionecrosis, what is that?
01:42:22 A That means necrotic tissue which has been
01:42:28 manifested many months after treatment.
01:42:32 Q And can you describe the wire implants that
01:42:37 Dr. Ashpole is talking about?
01:42:40 A Yes. You can put in wire catheters and load
01:42:46 those catheters with radioactive sources, loaded
01:42:54 directly into the tumor or the tumor bed.
01:42:58 Q Are those permanent or temporary?
01:43:03 A As he refers to it here, I believe he's talking
01:43:05 about temporary.
01:43:10 Q What does the dose distribution look like in --

Page 98

01:43:16 1 surrounding these wire implants?
01:43:18 2 A As we talked about earlier, it's sort of -- it
01:43:21 3 goes as 1 over R or 1 over R squared, but they're close
01:43:26 4 to the source. Since this is a wire only, if the tissue
01:43:30 5 is in contact with the source, the dose very close to it
01:43:32 6 is extremely high.
01:43:34 7 Q Then it would drop off as you move further
01:43:37 8 away?
01:43:37 9 A Yes.
01:43:39 10 Q So this would be a dose profile, sort of like
01:43:44 11 that that was seen with 7-A in the '204 patent?
01:43:57 12 MR. SU: Objection, form.
01:44:01 13 THE WITNESS: No, not really.
01:44:02 14 BY MR. MAURER:
01:44:02 15 Q How would it differ, 7-A, sir?
01:44:10 16 A Sorry, 7-A. It would differ in detail only, I
01:44:23 17 suppose, in that the way in which it would fall off with
01:44:29 18 distance is going to be different for the extended
01:44:32 19 source than it is for a line source in contact with the
01:44:37 20 tissue. But in both situations, the dose immediately
01:44:41 21 adjacent to the radiation source would be extremely
01:44:46 22 high.
01:45:02 23 Q Turn to page 336 of Ashpole, and about halfway
01:45:08 24 down in the right-hand column there is a paragraph
01:45:14 25 starting, Interstitial radiation...

Page 99

01:45:18 1 A Yes.
01:45:18 2 Q It again talks about late radionecrosis.
01:45:20 3 Is that the same radionecrosis that Dr. Ashpole
01:45:27 4 was saying was a form of radionecrosis, that Dr. Ashpole
01:45:30 5 is discussing on the first page?
01:45:32 6 A Yes.
01:45:32 7 Q And he's discussing long-term implants.
01:45:37 8 Are these long-term implants he's discussing
01:45:39 9 here the same type of the wire implants he discusses on
01:45:43 10 the first page?
01:46:04 11 A I think they are the same. I'm not sure
01:46:07 12 whether they are permanent implants or not that were
01:46:09 13 used in this case. I think maybe they were permanent
01:46:12 14 implants.
01:46:13 15 Q Would looking at the Gutin and Saleman article
01:46:16 16 help you answer that question?
01:46:17 17 A It would.
01:46:18 18 MR. MAURER: Let me mark as Exhibit Number 7 an
01:46:26 19 article by Gutin which is entitled -- or starts, A
01:46:32 20 coaxial catheter system for afterloading radioactive
01:46:37 21 sources.
01:46:37 22 (Plaintiff's Exhibit 7 was marked for
01:46:37 23 identification by the Court Reporter.)
01:46:37 24 BY MR. MAURER:
01:46:49 25 Q My first question to you is, can you compare

Page 100

01:46:52 1 the date and citation in the title of this article with
01:46:57 2 the one cited as a reference in Dr. Ashpole's article
01:47:02 3 and be sure that it's the same thing?
01:47:06 4 A It is.
01:47:09 5 Q And it's only two pages long, but I guess the
01:47:13 6 question for you is, is this a removable or permanent
01:47:17 7 catheter system?
01:47:19 8 A This is removable.
01:47:22 9 Q So let me give you then -- you can put that to
01:47:26 10 one side. Let me give you Exhibit Number 8.
11 (Plaintiff's Exhibit 8 was marked for
12 identification by the Court Reporter.)
01:47:35 13 BY MR. MAURER:
01:47:45 14 Q Before we do that, was that Gutin article the
01:47:48 15 one cited by Dr. Ashpole?
01:47:50 16 A You asked me that.
01:47:51 17 Q Did you say yes?
01:47:52 18 A Yes.
01:47:53 19 Q Now, I've given you what is marked as Exhibit
01:47:57 20 8.
01:47:58 21 Is it Saleman or Saleman?
01:48:06 22 A I'm not sure.
01:48:08 23 Q Is this the article that's referenced by
01:48:11 24 Dr. Ashpole on page 336?
01:48:24 25 A Yes.

Page 101

01:48:27 1 Q If you turn in Saleman to Figure 4, does this
01:48:38 2 show the device of Saleman?
01:48:41 3 A Yes, that's after loading catheter system.
01:48:44 4 Q Does that mean it's removable?
01:48:46 5 A Yes.
01:48:50 6 Q As long as we've got this article in front of
01:48:53 7 you, will you turn to Figure 5? In particular, I want
01:48:59 8 to look at 5D.
01:49:04 9 Do you see where I am?
01:49:05 10 A M-hm.
01:49:07 11 Q What does Figure 5D show?
01:49:17 12 A It shows a catheter with dummy seeds inserted.
01:49:29 13 Q This is the same sort of dummy source train
01:49:32 14 that Ashpole was talking about in calculating his doses?
01:49:35 15 A Yes.
01:49:36 16 Q If you look at the next page, which is page 146
01:49:39 17 in the upper left-hand corner of Exhibit 8, there are
01:49:47 18 two, I guess, radiographs there?
01:49:47 19 A M-hm.
01:49:48 20 Q And they are described on the bottom of page
01:49:52 21 147. You may or may not need to refer to that
01:49:58 22 description.
01:49:58 23 But my question is, what does Figure 6 show,
01:50:01 24 the image on page 146 -- the images on page 146?
01:50:32 25 A It shows a lateral and an anterior/posterior

Page 102

01:50:37 1 X-ray of the patient with the dummy seed positions and
01:50:49 2 calculated dose surfaces.
01:50:53 3 Q Looking at Figure 6, one of these is from the
01:50:59 4 side and one of them is from the back; is that accurate?
01:51:02 5 A One is from the side and one is from the front,
01:51:05 6 it says.
01:51:06 7 Q You can tell I did not go to medical school.
01:51:09 8 Which one is from the side and which is from
01:51:11 9 the front?
01:51:12 10 A The top is from the side.
01:51:14 11 Q And in the top one, there are a series of small
01:51:21 12 dashed lines.
01:51:22 13 Is that the dummy source train there?
01:51:27 14 A Well, I have to make sure that we're looking at
01:51:29 15 the dummy as opposed to the real seeds.
01:51:37 16 Q I don't mean to be that specific in my
01:51:39 17 question, so let me modify it.
01:51:41 18 A Those are the locations of radioactive seeds
01:51:45 19 inside the catheters.
01:51:48 20 Q And the same thing is true for the small dashed
01:51:52 21 indications inside the isodose curves on the bottom one?
01:51:57 22 A That's right.
01:51:58 23 Q Let me ask you to turn back two pages to Figure
01:52:01 24 3.
01:52:08 25 What does Figure 3 depict?

Page 103

01:52:22 1 A It shows one slice of a three-dimensional CT
01:52:25 2 scan, the one transaxial slice with superimposed dose
01:52:34 3 surfaces, dose contours on the -- at the location of the
01:52:41 4 target.
01:52:43 5 Q In looking at the lower right-hand corner of
01:52:46 6 this -- of the slice, I guess, in the box, do you see
01:52:52 7 where I'm talking about where the isodose curves are?
01:52:56 8 A Yes.
01:52:56 9 Q Is it -- it appears that there are white
01:53:03 10 splotchy circles inside that portion of the CT scan.
01:53:08 11 What do those relate to?
01:53:13 12 A That would be part of the tumor which probably
01:53:16 13 the patient would have been given contrast prior to the
01:53:19 14 CT scan, and you would see contrasting --
01:53:24 15 Q What's the scale on the right-hand side of
01:53:25 16 Figure 3?
01:53:27 17 A Those are dose colors.
01:53:31 18 Q Is it possible that those white splotchy things
01:53:34 19 that we see in the right-hand corner of the CT scan are
01:53:38 20 actually the dose contours -- or the color dose contours
01:53:49 21 that correspond to the interstitial seeds?
01:53:50 22 A It is possible, but the quality of this
01:53:52 23 reproduction does not allow me to determine that.
01:53:55 24 Q I can't tell you.
01:53:56 25 A By reading it, I would be able to determine if

Page 104

01:53:59 1 they completely removed the tumor surgically prior to
01:54:02 2 this procedure. Then I think your guess is that -- the
01:54:07 3 same as mine, that it would be the doses.
01:54:11 4 Q Regardless of what this actually corresponds
01:54:14 5 to, if they were plotting the doses of the seeds in this
01:54:23 6 configuration, you would expect to see -- a person of
01:54:28 7 ordinary skill in the art would see a very high dose
01:54:32 8 near the interstitial seeds?
01:54:34 9 A Correct.
01:54:35 10 Q The same as with a wire, but, in this case,
01:54:37 11 they are just a bunch of point sources?
01:54:40 12 A That's right.
01:54:50 13 Q Let's go back to Ashpole. Put that to the
01:54:53 14 side.
01:54:54 15 On page 333, the front page of Ashpole again,
01:54:56 16 the advantages that he's talking about here are
01:55:09 17 advantages with respect to avoiding radionecrosis caused
01:55:14 18 by devices of the configuration of the tape of Saleman
01:55:19 19 and Gutin that we just looked at?
01:55:22 20 A Right. From reading Ashpole, a person of
01:55:29 21 ordinary skill in the art would understand that one of
01:55:32 22 the ways that Dr. Ashpole achieves this advantage is by
01:55:35 23 spacing the radiation source in his device farther away
01:55:39 24 from the tissue than was done in those prior devices.
01:55:43 25 Correct.

Page 105

01:55:44 1 Q Just like we discussed with respect to Figure
01:55:48 2 7, in the graphs at 7-D?
01:55:53 3 A Right.
01:55:55 4 Q Let's go to page 336 of Ashpole, and in
01:56:06 5 particular, I want to talk about the first full
01:56:10 6 paragraph, which we discussed briefly earlier in your
01:56:14 7 deposition, that starts, The configuration of the
01:56:16 8 balloon...
01:56:18 9 A Okay.
01:56:19 10 Q Do you see where I am?
01:56:20 11 A M-hm.
01:56:21 12 Q And in that sentence, it talks about a dose
01:56:24 13 distribution.
01:56:26 14 What do you understand dose distribution there
01:56:28 15 to be referring to?
01:56:32 16 A The change of dose as a function of distance
01:56:39 17 from the source.
01:56:44 18 Q And in particular, this dose distribution is
01:56:47 19 talking about the change in dose from the surface of the
01:56:52 20 balloon into the target tissue?
01:56:55 21 A Yes.
01:56:57 22 Q And Dr. Ashpole uses the modifier "acceptable"
01:57:01 23 before that dose distribution.
01:57:04 24 How would a person of ordinary skill in the art
01:57:07 25 understand "acceptable dose distribution" as used by

Page 106

01:57:13 Dr. Ashpole there?
01:57:13 A I believe that person would understand that he
01:57:16 meant that the intervening tissues between the surface
01:57:21 of the cavity and the depth of the prescription dose
01:57:26 would receive acceptable doses.
01:57:33 Q "Acceptable" meaning what?
01:57:35 A Doses low enough they would not likely produce
01:57:37 radionecrosis.
01:57:42 Q And Dr. Ashpole later on in that paragraph
01:57:45 discusses -- this is about halfway down -- unacceptably
01:57:52 high doses close to the sources.
01:57:55 A Yes.
01:57:57 Q What unacceptably high doses be those that
01:58:00 would cause radionecrosis?
01:58:01 A Yes, that would be my opinion.
01:58:06 Q You discussed the inverse square wall -- I'm
01:58:10 sorry. Dr. Ashpole discusses the inverse square in
01:58:13 here?
01:58:14 A Yes.
01:58:16 Q With respect to the Ashpole source train, as
01:58:21 we've -- as you understand it now, having been referred
01:58:23 to Ashpole again, would the Ashpole source train be
01:58:27 considered to be a linear source or a point source or a
01:58:32 series of point sources for purposes of calculating the
01:58:35 dose distribution --

Page 107

01:58:39 MR. SU: Objection, form.
01:58:39 BY MR. MAURER:
01:58:41 Q -- or something else?
01:58:41 A It would be a series of point sources.
01:58:46 Q Would the best way to approximate that be as a
01:58:50 line source or as a point source?
01:58:55 A Very likely a line source would be a better
01:58:57 approximation.
01:58:59 Q Is there a rule of thumb, quick and dirty way
01:59:03 to calculate the dose for a line source at any
01:59:08 particular point?
01:59:10 A No, not really. Not quick and dirty. That's
01:59:14 why I believe that he is using the quick and dirty
01:59:18 approximation that it's a single point source.
01:59:23 Q Have you -- for line sources that fall within
01:59:29 the five to ten distance that we talked about earlier
01:59:35 with respect to not acting as a point source, that's
01:59:39 where this question is going. Do you understand that?
01:59:41 A Yes.
01:59:42 Q For those types of line sources, have you ever
01:59:46 approximated what the dose is by using a 1 over X
01:59:51 calculation instead of 1 over X squared?
01:59:55 MR. SU: Objection, form.
01:59:59 THE WITNESS: My answer would be no, because
02:00:00 it's far better to break up the line into a -- a better

Page 108

02:00:07 approximation is a series of sources, each of which
02:00:10 gives you 1 over R squared.
02:00:11 BY MR. MAURER:
02:00:15 Q In that section that we're talking about in
02:00:18 Dr. Ashpole's article, he talks about -- this is the
02:00:24 second sentence now -- the inverse square relationship,
02:00:26 it starts --
02:00:29 A Yes.
02:00:33 Q -- between the absorbed dose and distance from
02:00:34 the source results in a -- in the larger-the-balloon
02:00:38 diameter, the greater the relative dose at prescribed
02:00:41 distance from the balloon surface.
02:00:42 Do you see that?
02:00:43 A M-hm.
02:00:44 Q What is the relative dose that he's talking
02:00:47 about there?
02:01:02 A I assume he's talking about the dose relative
02:01:04 to the surface.
02:01:05 Q Would the relative dose that he's discussing
02:01:08 there be the dose at the prescription distance over the
02:01:12 dose at the balloon surface? It's not the most
02:01:35 clearly-worded sentence, I'll give you that.
02:01:38 A No, it's definitely not.
02:01:40 He seems to be saying it backwards, which is
02:01:43 that for a given dose at the surface, the dose at the

Page 109

02:01:47 prescription depth would be higher for a larger
02:01:51 diameter, which is a correct statement, but not the way
02:01:56 you normally say it.
02:01:57 Normally, you say for a fixed dose at a
02:02:00 distance -- at a prescription distance from the wall,
02:02:03 the dose at the surface would be higher or lower.
02:02:10 Q Would -- a person of ordinary skill in the art
02:02:12 would understand if they took time to read that through
02:02:15 is that if you have a larger balloon, there is less of a
02:02:20 gradient between the dose at the surface to the dose at
02:02:23 the prescription depth as compared to if you have a
02:02:26 smaller balloon?
02:02:27 A Correct.
02:02:39 Q Dr. Ashpole says that that configuration of the
02:02:41 balloon plays a key role in producing an acceptable dose
02:02:45 distribution?
02:02:47 MR. SU: Objection, form.
02:02:50 THE WITNESS: I would say the diameter of the
02:03:00 balloon plays a key role.
02:03:01 BY MR. MAURER:
02:03:03 Q Because the larger the diameter of the balloon,
02:03:05 the lower the difference in the dose of the surface to
02:03:13 the dose at the depth?
02:03:14 A Correct.
02:03:19 Q In fact, Dr. Ashpole says in this section you

Page 110

02:03:21 should not let the balloon get below a certain amount,
02:03:25 because if you do that, then the dose distribution is
02:03:29 going to be too great?
02:03:30 A The dose at the surface would be too great.
02:03:33 The ratio of that dose would be -- the dose at the
02:03:37 surface would be so much higher, that it's unlikely you
02:03:41 could put the needed dose at a depth without exceeding
02:03:45 the acceptable dose at the surface.
02:04:02 Q Which is more likely to cause necrosis, a dose
02:04:10 distribution like that that you would receive from the
02:04:16 wire catheter-type devices like we looked at in Gutin
02:04:21 and Saleman or the Ashpole device?
02:04:27 A Which is likelier to create radionecrosis?
02:04:32 Q Yes.
02:04:32 A I think the former.
02:04:32 MR. SU: Objection, form. Go ahead.
02:04:33 BY MR. MAURER:
02:04:34 Q The wire catheter device?
02:04:36 A The wire catheter device.
02:04:38 Q Let's go back to Exhibit 1. Look at paragraph
02:04:50 17.
02:04:54 A Yes.
02:04:56 Q You agree that Dr. Ashpole is not saying that
02:05:00 in all cases you want a 2.5-centimeter diameter, but
02:05:05 he's describing what should be the lower limit on the

Page 111

02:05:08 balloon diameter?
02:05:09 A Right.
02:05:11 Q And the reason that a person of ordinary skill
02:05:13 in the art would understand him to be doing so is to
02:05:15 avoid the unacceptably high doses near the source?
02:05:20 A Right.
02:05:31 Q In paragraph 17, the third sentence, Ashpole
02:05:34 does not teach changing the balloon diameter after
02:05:38 implantation.
02:05:40 You mean Ashpole does not teach changing the
02:05:45 balloon diameter after implantation and its initial
02:05:49 inflation; is that right?
02:05:50 A That's correct.
02:05:51 Q You're saying there is no -- Ashpole does not
02:05:54 teach a second round of inflation?
02:05:57 A That's right.
02:06:04 Q And then in the next sentence it says,
02:06:05 ...rather, it prescribes a minimum diameter to which a
02:06:09 balloon shall be inflated.
02:06:14 Do you mean by that that -- let me ask you a
02:06:18 different way.
02:06:19 What Ashpole actually says is that the balloon
02:06:22 should fill the cavity, but in no instance be under the
02:06:25 2.5-centimeter diameter? Is that more accurate?
02:06:29 A Yes.

Page 112

02:06:30 Q Was that a yes?
02:06:30 A Yes. Sorry.
02:06:38 Q Let's go to the '204 patent again, which is
02:06:41 Exhibit 2.
02:06:52 Is it your understanding of this patent that
02:06:55 the devices that are discussed in the patent, including
02:07:00 the ones that we looked at, such as Figure 7-B and 7-C,
02:07:05 that devices of that configuration can be used to treat
02:07:11 brain cancer?
02:07:16 A There is nothing which -- I don't recall
02:07:20 anything in here which would suggest that that could not
02:07:24 be done.
02:07:25 Q Let's actually look at column 7, line, it looks
02:07:29 like, 29 to 32.
02:07:41 A Yes.
02:07:42 Q Dr. Ashpole actually specifically says that the
02:07:44 devices of his invention -- I'm sorry. I said
02:07:48 Dr. Ashpole. Let me start that question again.
02:07:50 The inventors of the '204 patent actually say
02:07:53 that the devices they disclose in here can be used to
02:07:56 treat either brain or breast tumors?
02:07:59 A That's correct.
02:07:59 Q Especially useful for that treatment?
02:08:04 A Yes.
02:08:06 Q I want you to read to yourself, if you could,

Page 113

02:08:08 the portion of the patent that starts at line 7 -- I'm
02:08:11 sorry -- column 7, line 47.
02:08:15 A M-hm.
02:08:16 Q It goes up through column 8, line 6.
02:08:19 A Okay.
02:08:20 Q Could you read that to yourself, and I'll ask
02:08:21 you a question when you're done.
02:09:16 A Okay.
02:09:17 Q My question -- you may have to review it again
02:09:20 after I ask my question. My question to you, Dr.
02:09:22 Verhey, starting at page 47, line 7, going to column 8,
02:09:27 line 6, does that also describe the brachytherapy
02:09:30 technique set forth in Ashpole?
02:09:33 MR. SU: Objection, form.
02:11:35 THE WITNESS: Certainly similar. I'm not sure
02:11:37 exactly how to answer the question, because there is an
02:11:39 inner and outer balloon or volume described here which
02:11:45 is a bit different than what Ashpole was describing, but
02:11:49 the basic technique is very similar.
02:11:51 BY MR. MAURER:
02:11:52 Q If we -- if I ask you to assume that the
02:11:56 interspatial volume is satisfied by the source train --
02:12:01 or at least one of the beads in the source train and the
02:12:04 outer spacial volume is satisfied by the outer balloon
02:12:09 of Ashpole, then this section would square with Ashpole?

Page 114

02:12:13 A Very similar.
02:12:22 Q Let me go back to your report, which is Exhibit
02:12:23 1, your declaration.
02:12:32 In paragraph 18 you discuss certain doses.
02:12:36 Is it your opinion that a dose higher than 55
02:12:40 to 60 Gray would cause necrosis of brain tissue?
02:12:49 A It's my opinion that doses substantially higher
02:12:54 than that would be likely to cause radionecrosis. I
02:12:58 think this is considered to be approximately the
02:13:01 tolerance.
02:13:02 Q When you say "substantially higher," what do
02:13:04 you mean?
02:13:06 A Well, obviously, we're talking about 80 or 90
02:13:09 Gray, substantially higher than 60, I think. I think 60
02:13:14 is considered a relatively safe dose for small volumes
02:13:19 of brain tissue.
02:13:22 Q When you say "small volumes," you mean such as
02:13:26 that being treated by the device of Ashpole?
02:13:29 A Well, I guess that would also depend on the
02:13:32 diameter of the cavity, but yes.
02:13:38 Q What diameter would the cavity have to be in
02:13:40 order for the tissue to be treated by the device of
02:13:44 Ashpole to be not a small volume?
02:13:47 A I guess it would be a small volume.
02:13:51 Q Would 70 Gray cause necrosis in a small volume

Page 115

02:13:56 of tissue such as that being treated by the Ashpole
02:14:00 device?
02:14:01 A I think it's considered a very risky dose.
02:14:03 Q Is it your opinion that it would cause
02:14:08 necrosis?
02:14:08 A It's a probabilistic answer, but the
02:14:10 probability is increasing substantially relative to 60
02:14:14 Gray.
02:14:15 Q And it's substantially less than 80 or 90 Gray?
02:14:18 A Right.
02:14:25 Q And to some extent, as you said before, this is
02:14:27 a patient-specific issue?
02:14:28 A It is related to the patient's health and age
02:14:35 and genetics.
02:14:36 Q Do you agree that a physician attempting to
02:14:41 reduce necrosis in a patient, the goal of that physician
02:14:45 would be to reduce the dose received by the normal
02:14:49 tissue?
02:14:50 A Yes.
02:14:53 Q You say in paragraph 18, at line -- look at
02:14:58 that -- you have line numbers on this, which makes it
02:15:00 easier -- page 6, line 6, ...assuming a symmetric
02:15:06 distribution of source was in the balloon.
02:15:09 Do you see where I am?
02:15:10 A Yes.

Page 116

02:15:11 Q You say, assuming a symmetric distribution of
02:15:14 sources, because Ashpole can be used with an asymmetric
02:15:17 distribution spell; correct?
02:15:21 MR. SU: Objection, form.
02:15:24 THE WITNESS: That's not what I meant by that
02:15:25 statement.
02:15:25 BY MR. MAURER:
02:15:26 Q What did you mean?
02:15:28 A What I really meant was a distribution of
02:15:31 sources that can be approximated by a single source at
02:15:33 the center of the balloon.
02:15:37 Q In your opinion, does Ashpole teach the
02:15:39 possibility of using an asymmetric distribution of
02:15:42 sources in the balloon?
02:15:44 A No.
02:15:45 Q Let's take a look in Ashpole, at page 336 at
02:15:56 the bottom of the left-hand column. This is Exhibit 6.
02:16:04 Bottom of the left-hand column the paragraph that
02:16:07 starts, Cesium-137...
02:16:10 Are you in that paragraph?
02:16:11 A Yes.
02:16:12 Q The last sentence, A certain measure of dose
02:16:15 symmetrical versatility is possible in that the
02:16:17 positions of the active beads can be changed to produce
02:16:20 an isodose distribution specific to the geometry of the

Page 117

02:16:23 individual tumor base.
02:16:25 Did I read that correctly?
02:16:27 A Yes.
02:16:27 Q How would a person of ordinary skill in the art
02:16:30 understand that sentence?
02:16:33 A I would understand that sentence to say that if
02:16:36 you had, let's say, a spherical balloon inside an
02:16:42 elliptical cavity, that you would change the
02:16:45 distribution of sources so that you had more dose at the
02:16:50 long side of the long dimension of the cavity compared
02:16:54 to what you would have in the center of that cavity.
02:17:00 Q I want to make sure we're clear, so I will have
02:17:02 you draw that, if you can. I'll hand you a blank sheet
02:17:05 of paper that's been marked as Exhibit 9. I'll ask you
02:17:11 to draw what you just described.
02:17:11 A Okay.
(Plaintiff's Exhibit 9 was marked for identification by the Court Reporter.)
02:17:20 THE WITNESS: So I will draw an elliptical
02:17:21 cavity, which is certainly a possibility, and inside
02:17:25 that elliptical cavity I'm going to draw a spherical
02:17:30 balloon, which is in contact with the cavity at some
02:17:32 point. Then I'm going to show a source train in the
02:17:39 middle of that spherical cavity.
02:17:40 BY MR. MAURER:

Page 126

02:42:50 Q What was the surface dose in this study that
02:42:52 led to radiation necrosis of nine of the 54 patients?
02:43:00 A It says between 203 and 354 Gray, with a mean
02:43:06 of 314.
02:43:13 Q That's far larger than 70; correct?
02:43:15 A That's correct.
02:43:18 Q Is that surprising to you?
02:43:20 A No.
02:43:21 Q Why not?
02:43:22 A Because, if I'm not mistaken, these -- the
02:43:33 radiation was left in place for a significant period of
02:43:35 time. I have not found the actual answer here, it may
02:44:52 be here, in terms of how long they left it in place.
02:44:57 But the point is, a Gray is very different
02:45:03 depending on the way -- the duration of the time which
02:45:06 that radiation was delivered. If it's delivered
02:45:10 continuously over a period of time of days or weeks or
02:45:13 months, as in some cases with permanent implants, the
02:45:20 radiation tolerance in terms of Gray is very different
02:45:27 in that configuration than it is for radiation delivered
02:45:28 in a few short fractions either with external or with
02:45:35 sources.
02:45:36 So it's very difficult and is really impossible
02:45:40 to compare that number with a number that we're talking
02:45:44 about before. It's a big number, but so is the number

Page 127

02:45:51 that is calculated for, as an example, permanent seed
02:45:55 implants in the prostate. You calculate the doses and
02:45:59 they are enormous, because they are left in place.
02:46:06 Q So this goes back to your answer at the
02:46:09 beginning of the day where you told me it's not just the
02:46:11 dose; it's also the volume of tissue in the dose rate
02:46:15 that are important in determining what the cause is of
02:46:19 the necrosis?
02:46:21 A Right.
02:46:22 Q Fair enough. Let me just point you to the
02:46:24 bottom of page 376 before we leave this behind.
02:46:34 On the right-hand column, bottom of page 376,
02:46:37 it says that the prescription dose for each patient was
02:46:41 a total dose of 60 Gray at a 1-centimeter depth to be
02:46:46 delivered at a rate of 40 to 60 centigrade per hour.
02:46:49 Does that tell you what you need to know with
02:46:52 respect to how long it took to deliver this dose?
02:46:56 A Yes. So -- it's 100 hours, so it must have
02:46:58 been -- more than 100 hours, 100 to 150 hours, so it
02:47:03 would have been days, many days.
02:47:12 Q You can put that aside.
02:47:20 Before you put Exhibit 10 to the side, will you
02:47:23 turn to the last page -- I'm sorry -- page 382.
02:47:33 A Yes.
02:47:33 Q The bottom of the right-hand column, starting

Page 128

02:47:36 about four lines up, there is a sentence that reads,
02:47:39 There is no absolute upper limit in the size of the
02:47:42 pre-operative tumor because the brain collapses around
02:47:45 the resectioned cavity when the lesion is completely
02:47:48 removed.
02:47:49 Do you see that?
02:47:50 A Yes.
02:47:51 Q Do you have any reason to doubt the statement
02:47:53 that the pre-op -- that the brain collapses around the
02:47:58 resectioned cavity when a lesion is removed?
02:48:02 A No. I think we talked about it before, the
02:48:05 extent to which that happens and the speed at which it
02:48:08 happens, I think, is variable.
02:48:10 (Plaintiff's Exhibit 11 was marked for
02:48:10 identification by the Court Reporter.)
02:48:10 BY MR. MAURER:
02:48:19 Q Now you can really put it to the side. I'll
02:48:30 give you Exhibit 11.
02:48:31 Have you seen this document before?
02:48:50 A No.
02:48:51 Q It's an article entitled, GliaSite
02:48:52 Brachytherapy Boost as Part of Initial Treatment of
02:49:01 Glioblastoma Multiform.
02:49:01 A Yes.
02:49:12 Q What is a boost treatment?

Page 129

02:49:13 A It means --
02:49:13 MR. SU: Object to the form.
02:49:15 THE WITNESS: It means that the patient
02:49:18 presumably received external beam radiation to some dose
02:49:23 in the vicinity -- including this tumor site, and that
02:49:27 this would be boosting the region of the surgical cavity
02:49:32 itself to a higher dose.
02:49:34 BY MR. MAURER:
02:49:36 Q Let me ask you to turn to page 163. In the
02:49:47 left-hand column, four lines up from the bottom, there
02:49:50 is a sentence that starts, The inflatable balloon...
02:49:54 Do you see that?
02:49:56 A What page did you say?
02:49:57 Q Page 163.
02:49:59 A Sorry. I thought you said 162.
02:50:02 Q Bottom right --
02:50:04 A Right. Okay.
02:50:04 Q -- bottom left-hand column, The inflatable
02:50:07 balloon allows the brain tissue at greatest risk of
02:50:11 recurrence, that is, the tumor bed to collapse down
02:50:14 around it for a tight, conformal fit. This, in turn,
02:50:18 provides a close proximation of the balloon surface to
02:50:22 the resection margin and allows the delivery of a
02:50:25 radially-uniform radiation dose to the residual tumor
02:50:29 and/or to the margins of the resectioned cavity.

Page 130

02:50:32 Did I read that correctly?
02:50:34 A You did.
02:50:34 Q Do you have any reason to disagree with the assertion that after resection of a tumor, that the tumor bed would collapse down on a balloon in the brain?
02:50:48 MR. SU: Objection. Again, same objection to asking questions about Exhibit 11, as with 10 and 7 and eight. These are articles that the witness has not 8 before. And so I object to questions that focus on particular areas without giving the witness a chance to read the entire article.
02:51:09 BY MR. MAURER:
02:51:13 Q I'm not asking you -- to be clear, Dr. Verhey, not in the context of this article, just that statement alone.
02:51:18 Do you have any reason to disagree with that statement?
02:51:20 A If I were involved in this study, I would certainly want to ask the question of the investigators about the extent and speed of which this collapse happens.
02:51:35 Q You don't know sitting here today the extent and speed to which it happens, but you would want to find out?
02:51:42 A I would want to find out, yes.

Page 131

02:51:44 Q It could be that it happens quickly as a conformal collapse around the balloon?
02:51:48 A It could be.
02:51:50 Q You can put that to the side.
02:51:58 MR. MAURER: Let's mark as Exhibit 12 a patent bearing the number 5,913,774.
02:52:10 (Plaintiff's Exhibit 12 was marked for identification by the Court Reporter.)
02:52:17 BY MR. MAURER:
02:52:27 Q Have you seen this document before?
02:52:28 A Yes.
02:52:30 Q In fact, this is the second of the two references that you discussed in detail in Exhibit 1, which is your declaration?
02:52:34 A Right.
02:52:36 Q So you should pull out Exhibit 1, since we'll be discussing that as well, please.
02:52:37 In Williams, you have focused on the device of Figure 3. Could you turn in Exhibit 12 to Figure 3?
02:53:03 A Yes.
02:53:06 Q Do you agree, Dr. Verhey, that the device of Figure 3 is designed to treat tissue surrounding a surgical extraction?
02:53:14 A Yes.
02:53:17 Q And do you agree that this device has an expandable outer balloon?
02:53:21 A Yes.
02:53:25 Q And that this device is configured to fill the cavity from which the tumor has been resected?
02:53:28 A I only have to check to see if I agree with the language. This stuff is tricky.
02:53:30 Q Sure, please do.
02:53:34 A Well, the words I see here don't quite say that. It says --
02:53:36 Q Where are you?
02:53:36 A I'm sorry. I'm on column 9, line 49, I suppose.
02:53:39 It just says, ...introducing a treatment fluid into the treatment fluid receptacle so that the balloon is inflated such that the proliferative disorder is treated.
02:53:47 Q Let me refer you, Dr. Verhey, to column 7, line starting at line 41, that section.
02:53:50 A Okay.
02:53:56 Q Does that section tell a person of ordinary skill in the art that the device of Figure 3 is configured to fill the reception cavity?
02:55:44 A It states that the shape of the balloon should conform to the shape of the surgical cavity prior to inflation as much as possible so that when it's

Page 132

02:55:47 inflated, it approximates the shape of the surgical cavity.
02:55:50 It also talks about a different situation in which compression is desirable. For example, when treating restenosis of a blood vessel, the balloon can be inflated to a size large enough to compress the excess tissue while also providing chemotherapy, brachytherapy or the like to treat the lesion.
02:55:51 So in that example, it's inflated purposely to compress.
02:55:57 Q I guess the question is, does Figure 3 include devices -- in the understanding of a person of ordinary skill in the art, does it include devices in which the balloon is configured to fill the cavity?
02:56:01 A I would say that it is a balloon which approximately fills the cavity as shown in Figure 3.
02:56:04 Q Why do you say approximately fills the cavity as shown in Figure 3?
02:56:08 A Well, it says, for instance, on line 51, column 7, it says, Thus, when a radioactive treatment fluid is introduced in the device, for instance, by injection, the inflatable treatment device is inflated to a volume not substantially greater than the volume of the body cavity in which the device has been placed, thereby avoiding any substantial compression or distortion of

Page 134

03:00:07 normal tissue.
03:00:12 Q How do you understand the phrase "inflated to a
03:00:15 volume not substantially greater than the volume of a
03:00:19 body cavity in which it's been placed"?
03:00:28 A Its shape and dimensions are selected in order
03:00:32 to closely approximate the surgical cavity in its
03:00:38 natural volume.
03:00:43 Q This includes inflating the device to a volume
03:00:47 that is greater than the volume of the cavity but not
03:00:51 substantially greater than the volume of the cavity?
03:00:54 A It could, yes.
03:00:55 Q And a person of ordinary skill in the art would
03:00:59 say that that description can apply to the description
03:01:01 in Figure 3?
03:01:02 A Yes.
03:01:03 Q And when Figure 3 is configured, that outer
03:01:07 balloon is going to contact the tissue in the cavity?
03:01:14 A Certainly at some places.
03:01:18 Q It would touch the tissue of the cavity, why do
03:01:23 you say at some places?
03:01:26 A I would expect that in general, the shape of
03:01:29 the balloon will not perfectly conform to the shape of
03:01:33 the cavity, in which case there would be portions of the
03:01:38 cavity that are not in contact with the balloon.
03:01:41 Q Would a person of ordinary skill in the art

Page 135

03:01:43 understand that the balloon of the device of Figure 3
03:01:47 could contact the walls of the cavity --
03:01:51 A Yes.
03:01:52 Q -- substantially?
03:01:55 A Yes.
03:01:55 Q Completely?
03:01:56 A Yes, it could.
03:01:59 Q Based on this description, a person of ordinary
03:02:01 skill in the art would understand that in one of its
03:02:05 configurations, the device of Figure 3 -- the balloon of
03:02:10 the device of Figure 3 could be touching substantially
03:02:13 completely all of the wall of the cavity?
03:02:17 A I think they would understand that the
03:02:21 greater -- the greatest extent to which that can be true
03:02:29 is desirable.
03:02:33 Q That's one of the reasons that the inventors of
03:02:36 the '774 patent said that in the case where you don't
03:02:40 want to compress the tissue, even where you're not
03:02:44 trying to compress the tissue, you inflate the balloon
03:02:47 to a volume that is not substantially greater than the
03:02:53 volume of the cavity; correct?
03:02:57 A Yes.
03:03:06 Q Because inflating the balloon to a volume that
03:03:09 is greater than the cavity but not substantially greater
03:03:11 than the cavity increases the conformance of the balloon

Page 136

03:03:15 to that cavity?
03:03:17 A That's correct.
03:03:18 MR. SU: Objection, form.
03:03:20 THE WITNESS: Yes.
03:03:20 BY MR. MAURER:
03:03:23 Q And in the device of Figure 3, you agree there
03:03:27 is a radiation source disposed within this outer
03:03:31 balloon?
03:03:48 MR. SU: Objection, form.
03:03:49 BY MR. MAURER:
03:03:53 Q If you want, I can direct you to your
03:03:54 declaration.
03:04:03 A Go ahead.
03:04:04 Q In your declaration, at paragraph 22, which is
03:04:15 at the top of page 7, sort of -- the paragraph number is
03:04:17 cut off by the caption --
03:04:19 A Yes.
03:04:19 Q -- you state in the second sentence, The outer
03:04:25 balloon is filled with a chemotherapeutic fluid and the
03:04:28 inner balloon is filled with a radioactive fluid.
03:04:32 A That's right. I think it's backwards from what
03:04:34 you asked.
03:04:35 Q I'm sorry.
03:04:37 A I thought you asked me whether the outer
03:04:39 balloon was filled with radioactive fluid.

Page 137

03:04:41 Q I did not mean to. Let me try this again so
03:04:44 the record is clear.
03:04:45 In the device of Figure 3, do you agree that
03:04:47 there is a radioactive source inside of the outer
03:04:52 balloon?
03:04:55 A Yes, this is correct.
03:04:57 Q And that radioactive source in Figure 3 is the
03:05:01 balloon that I believe is labeled 40 in that figure?
03:05:05 A Yes.
03:05:09 Q And Figure 3 shows that the inner balloon,
03:05:11 balloon 40, is asymmetrically arranged in the outer
03:05:17 balloon?
03:05:18 MR. SU: Objection, form.
03:05:22 THE WITNESS: It's not symmetric with the outer
03:05:24 balloon sphere -- the sphere of the cavity of the outer
03:05:28 balloon, that's correct, in that figure.
03:05:29 BY MR. MAURER:
03:05:38 Q Can you, using the red pen on Figure 3, draw
03:05:41 the isodose curve or curves that would result from
03:05:44 having a radioactive fluid inside the inner balloon of
03:05:47 Figure 3?
03:06:01 MR. SU: Objection to form, incomplete
03:06:02 hypothetical.
03:06:02 BY MR. MAURER:
03:06:10 Q Do you agree that that dose distribution is

Page 138

03:06:13 asymmetric with respect to the outer balloon?
03:06:17 A Yes.
03:06:24 Q Is it true, Dr. Verhey, that as of 1999, at
03:06:29 least 1999, prior to inflating that inner balloon with a
03:06:34 radioactive fluid, the profile that would be -- would
03:06:40 result from doing so would have been calculated?
03:06:44 A Yes.
03:06:46 Q That's been true for decades now?
03:06:49 MR. SU: Objection, form.
03:06:51 THE WITNESS: For a long time.
03:06:52 BY MR. MAURER:
03:06:56 Q In your declaration, in paragraph 24, at line
03:07:02 12 -- at the end of line 12, you have a sentence that
03:07:08 starts, If the inner balloon has an asymmetry relative
03:07:13 to the outer balloon --
03:07:14 Do you see that?
03:07:14 A Yes.
03:07:15 Q -- that asymmetry is fixed by the geometric
03:07:19 constraints of the device, and, therefore, the position
03:07:21 of the inner balloon cannot be altered to provide
03:07:24 predetermined isodose curve -- it does not say curve.
03:07:34 Maybe it should, but it does not.
03:07:39 What do you mean asymmetry fixed by geometric
03:07:44 constraints of the device?
03:07:50 A What I mean by that is, Williams does in the

Page 139

03:07:54 indicate that the location of the center of the inner
03:08:00 balloon is something that can be varied on a
03:08:05 patient-to-patient basis. Therefore, the asymmetry you
03:08:11 achieve would be determined by where it is rather than
03:08:13 the asymmetry you may want to have on the basis of the
03:08:19 tissues surrounding the cavity.
03:08:29 Q Does the '142 patent require that the
03:08:33 asymmetric dose be able to be changed in a device?
03:08:42 MR. SU: Objection to form, calls for a legal
03:08:44 conclusion.
03:08:45 BY MR. MAURER:
03:08:48 Q Do you have an opinion on that?
03:08:52 A My opinion is that the '142 gives you a --
03:08:57 describes a device in which the asymmetry of the
03:09:04 resulting dose distribution can be managed by the
03:09:08 position of the sources in the catheters.
03:09:31 MR. MAURER: Let me mark as Exhibit Number 13
03:09:34 the '142 patent.
03:09:35 (Plaintiff's Exhibit 13 was marked for
03:09:35 identification by the Court Reporter.)
03:09:35 BY MR. MAURER:
03:09:49 Q Dr. Verhey, where does the '142 patent, Exhibit
03:09:54 13, describe a device in which the asymmetry can be
03:09:59 managed by the position of the radiation source in the
03:10:02 catheters?

Page 140

03:10:04 A This will take a minute.
03:10:05 Q Sure. Please.
03:11:02 A It's all over the place.
03:11:04 Q Okay. Let's start --
03:11:05 A Column 3, the first complete paragraph. In
03:11:13 other examples, the radiation source spaced apart is
03:11:18 solid radioactive particles disposed within the
03:11:21 apparatus volume and arranged to provide a predetermined
03:11:24 asymmetric isodose curve within the target tissue.
03:11:30 Q Does that describe a device in which the
03:11:31 position of the radioactive particles can be changed?
03:11:36 A Within the catheters, they could be changed.
03:11:46 Q Is that an example that's depicted in one of
03:11:48 the drawings?
03:13:15 A Figure 3 as an example -- wait a minute. Let
03:13:20 me see if 4 is a better example.
03:14:05 Probably 4 is -- the last paragraph of column
03:14:07 6.
03:14:08 Q Okay.
03:14:11 A An additional device 80 of the invention shown
03:14:17 in Figure 4 includes a radiation source 82 that is made
03:14:23 up of three wires, 84, 86, 88, each having a plurality
03:14:29 of solid radiation particles. Wire 86 is a straight
03:14:35 wire extending along the longitudinal axis 90 of the
03:14:39 device, while wires 84 and 88 each curve, as wire 34

Page 141

03:14:46 described above with respect to Figure 1. Wires 84 and
03:14:50 88 are coplaner resulting in an isodose profile 92 that
03:14:57 is similar to size. Dose profile 64 of Figure 3A, that
03:15:04 is, the isodose profile, will be symmetric in the plane
03:15:08 in which wires 84 and 88 are disposed, will have areas
03:15:12 of reduced dosage in areas transfers to that plain that
03:15:16 is in Figure 4 the directions into and out of the page.
03:15:21 As with the device 50 of Figures 3 and 3A,
03:15:25 device 80 can be configured with more or fewer wires,
03:15:29 84, 86 and 88, and can be provided in configurations
03:15:35 other than the depicted coplaner configuration in order
03:15:39 to desired asymmetric isodose profiles.
03:15:44 Q That is what that section says, Dr. Verhey. My
03:15:47 confusion is to how that describes a device in which the
03:15:53 asymmetry of the radiation profile can be managed by the
03:15:59 position of the wires and the catheters.
03:16:05 A Why is that confusing?
03:16:07 Q Isn't this section that you just read, isn't
03:16:11 that properly read that there is a device such as that
03:16:15 shown in Figure 4, or you can modify the device of
03:16:19 Figure 4 into another device by removing one or more of
03:16:26 the arms or the radioactive sources on those arms?
03:16:31 A Yes.
03:16:32 Q So what that passage is saying is that there
03:16:35 are a multiplicity of devices that fall within this

Page 142

03:16:42 description, but not that those devices themselves are
03:16:47 modifiable in order to manage the asymmetric profile?
03:16:52 A I believe there are a multiplicity of
03:16:56 embodiments of this invention which are being described,
03:16:59 not a multitude of different inventions or different
03:17:02 devices.
03:17:02 Q And do you agree that for the embodiment that
03:17:06 is shown in Figure 4, that the asymmetry is fixed by the
03:17:12 geometric constraints of that device?
03:17:16 A As well as by the activity of the sources
03:17:17 within the wires.
03:17:20 MR. SU: Objection, form.
03:17:21 BY MR. MAURER:
03:17:24 Q Is that a yes and --
03:17:27 A Yes.
03:17:30 Q And the device of Figure 3 is one in which the
03:17:34 asymmetry is fixed by the geometric constraints of the
03:17:37 device?
03:17:40 MR. SU: Objection, form.
03:17:42 THE WITNESS: It is fixed by both the location
03:17:46 and the activities of the sources in that device.
03:17:48 BY MR. MAURER:
03:17:52 Q And the device of Figure 3 of the '774 patent,
03:17:55 going back to Exhibit Number 12, is likewise --
03:18:01 according to your opinion, the asymmetry is fixed by the

Page 143

03:18:08 geometric constraints of the device; correct?
03:18:13 A I'm not sure I would agree with the "likewise"
03:18:16 statement you just said.
03:18:19 Q That's where I think we're having a disconnect,
03:18:21 Dr. Verhey.
03:18:22 A Yes.
03:18:23 Q What is it that you're trying to express in the
03:18:26 statement in paragraph 24 that we started this
03:18:28 conversation with that differentiates the embodiments --
03:18:32 admittedly, there are many of them -- in the '142 patent
03:18:38 from the embodiments of Figure 3 in the '774 patent?
03:18:42 A Figure 3 of '774, the shape of the isodose
03:18:52 distributions is completely fixed by the position of the
03:18:57 inner surface of the inner balloon, the position of the
03:19:03 inner balloon as well as the diameter. The -- excuse
03:19:08 me. Take that back.
03:19:10 The shape is determine purely by the location
03:19:12 of that inner balloon, nothing more, whereas, in '142,
03:19:21 the shape of the isodose lines can be modified by either
03:19:27 using different embodiments of this device or different
03:19:37 placement of the wires or different activities of the
03:19:42 individual wires in order to produce a particular,
03:19:46 desired asymmetric dosage region.
03:19:55 Q Let's go back to the '774 patent.
03:20:00 Can radioactive fluids of different activities

Page 144

03:20:03 be used in the device of Figure 3?
03:20:05 A Yes.
03:20:06 Q Can the balloon -- the inner balloon of Figure
03:20:11 3 be changed in its position in the outer balloon?
03:20:15 A It is not at all clear to me that it can.
03:20:18 Q Does the '774 patent discuss the use of
03:20:24 different sizes of balloons?
03:20:26 A Yes.
03:20:27 Q And would a person of ordinary skill in the art
03:20:30 understand that that applies to Figure 3?
03:20:33 A Yes.
03:20:34 Q And that it applies to the inner balloon as
03:20:39 well as the outer balloon?
03:20:41 A Yes.
03:20:43 Q So in using a different size inner balloon, you
03:20:46 can achieve a different asymmetric isodose profile in
03:20:52 Figure 3 of the '774 patent; correct?
03:20:56 MR. SU: Objection, form.
03:20:57 THE WITNESS: I have to expand on my answer,
03:21:00 yes.
03:21:00 The ratio of doses as an example between, let's
03:21:06 say, the bottom line of this figure here and a point on
03:21:12 the wall of the surgical cavity up at the top, that
03:21:17 ratio cannot be modified by using different activity
03:21:21 fluids because the shape of the dose distribution is

Page 145

03:21:25 determined by the geometry.
03:21:29 That ratio that you just described can be
03:21:32 modified by using different size balloons, though, to a
03:21:37 very minor extent. You can take an extended source and
03:21:43 turn it into a point source and make some changes in
03:21:53 that regard, but not in terms of sparing normal tissues
03:22:01 of particular interest to you, I don't believe the
03:22:05 versatility of changing the diameter of that balloon
03:22:08 would be accurate in a clinical sense.
03:22:10 Q Does the '142 patent require the sparing of
03:22:14 critical tissues?
03:22:16 A No.
03:22:21 MR. SU: Objection to form.
03:22:23 BY MR. MAURER:
03:22:31 Q Let's go back to the '142 patent. In Figure
03:22:37 1 --
03:22:44 MR. MAURER: We need to change the tape.
03:22:46 VIDEOGRAPHER: This is the end of videotape
03:22:47 number two. We are now going off the video record. The
03:22:49 time is 3:22 p.m.
(Recess Taken.)
03:25:27 VIDEOGRAPHER: This is the beginning of tape
03:25:29 number three. We are back on the video record. The
03:25:31 time is 3:25 p.m.
03:25:31 BY MR. MAURER:

Exhibit 32

IN THE UNITED STATES DISTRICT COURT

NORTHERN DISTRICT OF CALIFORNIA

SAN JOSE DIVISION

- - - - - - - - - - - - - - - - - x

HOLOGIC, INC., CYTYC :

CORPORATION and HOLOGIC, L.P, :

Plaintiffs, :

v. :

SENORX, INC., :

Defendant. :

- - - - - - - - - - - - - - - - - :CASE NO. 08-CV-0133 RMW

SENORX, INC., :

Counterclaimant, :

v. :

HOLOGIC, INC., CYTYC :

CORPORATION and HOLOGIC, L.P, :

Counterdefendants.:

- - - - - - - - - - - - - - - - - x

THIS TRANSCRIPT IS DESIGNATED HIGHLY CONFIDENTIAL

Friday, April 4, 2008

Video Deposition of COLIN G. ORTON, PH.D.

Commencing at 1:30 P.M.

DIGITAL EVIDENCE GROUP
1111 16th Street, NW Suite 410
Washington, DC 20036
(202) 232-0646

mischaracterizes his testimony. You can answer the question again.
A Yeah, can you answer -- ask -- well, repeat the question, and I -- I would like to answer it, if I can, if I may.
MR. COHN: Sure.
THE WITNESS: The physician is making this --
BY MR. COHN:
Q A physician tells you that -- that he believes the brain tissue is particularly sensitive to deformation and compression by the balloon, and that, therefore, it's not desirable to unduly deform or compress the brain tissue, in particular, in your experience would you have a basis to disagree with that physician?
A No.
Q Would you agree that in the device described in Ashpole the Ashpole device produces a mean dose rate at a given distance from the balloon surface by varying the position of active and inactive beads in the source train until a satisfactory isodose

curve to match the cavity shape is found?
A Can you repeat the -- it's a long sentence, there.
Q Sure. Well, let me -- let me point you to -- to the passage I have in mind, which is on page 335, column one, and if you'll indulge me a moment, if you look in column one of 335, just above the figure.
You would agree that the mean dose rate at a given distance from the balloon surface is performed by varying the position of active and inactive beads in the source train until a satisfactory isodose curve to match the cavity shape is found; do you see that statement?
A That's not one statement, here, it's -- it's -- it's abstracts from several statements, several sentences, there.
Q Okay. But let's go concretely.
A Right.
Q The sentence that begins, this is computed by; do you see that?
A Yes.
Q What is the "this" that's referred to

there?
A Okay, this represents -- as a -- as a medical physicist I can tell you, as a brachytherapy physicist I can tell you, that this represents that you can vary the positions of the active and the inactive beads of the source train to produce a satisfactory isodose curve to match the cavity shape.
And, coincidently, the total activity that's contained will produce a dose -- mean dose rate of 250 Gy centigrade per hour and the distance of .5 centimeters.
So it's a mixture of the distribution of the active and inactive seeds and the total number of active seeds, it's a mixture of both of those.
Q So is this saying that the mean dose rate and the distribution of that dose is -- is determined by varying the position of these active and inactive beads?
A Again, that's part of the answer. Also, the total activity of the active seeds, in addition to just getting a -- a satisfactory isodose curve, which is the position of the active and inactive seeds, the

total activity of the active seeds will give you the 250 centigrade per hour.
Q So -- and, again, I just want to understand this, that there's three things involved, there's a mean dose rate, an isodose shape, and a total activity; is that right?
MR. MAURER: Objection, vague.
A All three are interconnected.
Q And the determination of those three is -- well, strike that -- in -- in the Ashpole device those three quantities are determined by the position of the active and inactive beads in the source train; is that what this says, here?
A It doesn't say that the physician makes this decision, at all. Usually this is the work of a medical physicist.
Q Well, I think what I was asking is the -- regardless of who calculates it the total activity, the dose rate and the isodose shape, is determined by varying the position of active and inactive beads in the source train in this device; is that right?
A Yes.

Q Let me ask a question. If the cavity shape is spherical, in your view, if it's conformed to the shape of the balloon -- well, let's back up -- do you believe that the cavity in Ashpole is conformed to the shape of the balloon?
A Yes.
Q So the cavity would be spherical?
A No.
Q Okay, explain that?
A From the example shown, it's not spherical, it's elongated.
Q You would agree that the article here does not describe changing the diameter of the balloon after it's been implanted; is that correct?
A Oh, it -- it definitely does.
Q Where is that?
A When it's first implanted it's -- it's not expanded.
Q Okay.
A It's expanded later on, in order to create a roughly spherical cavity, so that the -- the distances can be measured in order to make these

calculations of dose rate and total -- and dose distribution.
Q Okay. Does Ashpole describe changing the diameter of the balloon once it's been inflated?
A Once it's been inflated?
Q Yes.
A He doesn't directly say that, as far as I could see, but he does say, on page 336, that the configuration of the balloon plays a key role in producing that acceptable dose distribution.
And as a person of ordinary skill in the -- in this field of brachytherapy I would interpret that as maybe meaning that it could be changed if the shape or the size of the balloon, initially, is not quite what was desired.
Q Does the Ashpole article disclose controlling the dose at the surface of the balloon so that it is not so high that it lethally damages healthy brain cells in contact with the surface of the balloon?
A Yes.
Q Where does it do that?

A Can you -- oh, I was going to ask you to tell me where it says this, you seem to be reading it.
Q I am just reading from my own outline.
A Oh, okay. Again, in that same sentence I was just reading, on page 336, and in the previous paragraph, it states, that we can now deliver an absorbed dose of 50 Gy of point five centimeters depth from the surface of the balloon, it goes onto say, this is of the same order of magnitude as used by others. So there's the dose.
The dose at the surface of the balloon depends on the number and arrangement of sources, as well as the balloon diameter, and can be as high as 70 Gy.
Q Where do you see 70 Gy?
A At the sixth line down on the right-hand column in page 30 --
Q Oh, I see.
A -- 336.
Q Is 70 Gy, in your view, a lethal dose or not?
MR. MAURER: Objection, vague.

A I really can't answer that, because these patients have been irradiated before, and this is a decision the physician makes who's doing the treatments whether the previous irradiation plus this new irradiation will be tolerable by the patients. And he makes the statement that -- that he believes that this will be tolerated by the patient.
Q If I told you that 70 Gy was a lethal dose -- well, you wouldn't take my word for it, let's strike that -- if a physician told that you 70 Gy was a lethal dose, and I would ask you to accept that for purposes of this question, you would agree that Ashpole does not disclose controlling the dose at the surface of the balloon so that it is not so high that it lethally damages healthy brain cells; right?
MR. MAURER: Objection to form, incomplete hypothetical.
A I don't think I could answer that, as a physicist, looking, reading this, it's -- it's maybe what he had in mind. I have no way of knowing.
Q You would agree that the article says that the dose at the surface of the balloon can be as high

as 70 Gy?
A Correct.
Q Can you go to the first page of the article, in the right-hand column, in the second paragraph, it says, the limited tolerance of normal brain has restricted the maximum permissible dose to about 55 to 60 Gy.
Doesn't that suggest that the normal brain cannot tolerate more than 55 to 60 Gy?
A We need to take into account a number of other factors when we talk about tolerance of brain tissue, and any other tissue, a number of factors, the volume of brain that's irradiated, the dose rate that the radiation is delivered at, and the number of fractions that are delivered and, one more, what previous radiation therapy has been delivered to those tissues.
So, to answer your question, it depends on too many factors that are not defined here, in this article, for these other studies.
Q So according to this article it could be that 70 Gy is lethal or it could not be, it depends on

the circumstances?
A Ashpole states that it is not.
Q Where does he say that?
A First of all, he makes the statement that the balloon diameter has to be such that the maximum dose at the surface of the balloon can be as high as 70 Gy.
He goes onto say, in the paragraph below, and I'll quote it, the balloon also acts as a buffer -- as a buffer that absorbs the unacceptably high doses close to the sources.
So the indication is, here, that by using the balloon and restricting the dose to 70 Gy you're no longer unacceptably high in the dose.
And then, reading in the next two paragraphs, below, the statement is made that, interstitial irradiation with long-term implants has been used in glioma, but a major problem has been a high incidence of late radionecrosis necessitating further surgical invention to decrease intercranial pressure. This is the late reaction that we're talking about trying to avoid. This problem will be

avoided by a removable catheter system such as ours.
So he's indicating to me, as a reader of this article, that he believes this is safe and that you're not exceeding the tolerance and producing late radionecrosis and necessitating further surgical intervention.
Q The interstitial irradiation with long-term implants, that's mentioned in that paragraph, what is that referring to?
A It looks like he gives two references here. And I would need to look up those references to know exactly what interstitial implants we're talking about. There are many different ways of doing interstitial brachytherapy.
Q Do you know which one he's referring to?
A He refers to two, Gutin and Dormandy, 1982, and Saleman, et al., 1986.
Q Do you know the interstitial irradiation with long-term implants that's discussed in those articles?
A No.
Q Do you have any understanding what

interstitial radiation with long-term implants is referring to in that sentence?
A There are a number of different things it could be referring to, for instance, it could be referring to permanent implants, where you put a radio isotope in, it decays over several months, and you just leave it there for the life of the patient, that's one way to treat these cancers.
Another way is you put tubes, multiple tubes in, multiple, and we call these interstitial implants, and -- and you might do low dose rate brachytherapy, which spreads a treatment over about a week, or you might do high dose rate brachytherapy, where you give a number of short fractions, it's another possibility.
A third possibility is you put a single source -- high -- relatively high activity source into the center of where you think the tumor is, and you -- so there are many different types of -- of long-term implants that one might use.
And I don't know what the term long-term implants means without reading the articles. Do they

mean seven days or do they mean the lifetime of the patient? It's not clear.

Q Are any of the interstitial radiation techniques with long-term implants removable, like the system shown in Ashpole?

A Usually, when you refer to long-term implants, you're probably referring to low dose rate instead of Ashpole actually uses medium dose rate, which is different, or you're referring to permanent implants that are there for the lifetime of the patient.

So it's not clear to me that that could be equivalent to what Ashpole has been doing in terms of this term, long-term implants.

Q Sure.

A I would think of Ashpole as a short-term implant.

Q Okay, in that context, you would agree that the interstitial irradiation with long-term implants is not a removable system like in Ashpole?

MR. MAURER: Objection to form.

A It could well be a removable low dose rate

system.

Q Are any of the interstitial radiation with long-term implant techniques that you think are discussed in this article implanted into an already debulked tumor?

A I have no way of knowing without reading the articles.

Q They may or they may not be?

A They may or may not be.

Q What is a debulked tumor?

A A debulked tumor refers to a tumor that the surgeon has removed part of that tumor and has probably left behind, because he doesn't want to take too much normal brain tissue, probably left behind some tumor.

Q And hence the need for irradiation; is that correct?

A Yes.

Q If we could look at page 336?

A Yes.

Q Of Ashpole, at column one?

A Yes.

Q The last full paragraph in that column, it begins with Caesium-137; do you see that paragraph?

A Yes.

Q And then, at the last sentence of that paragraph says, a certain measure of dose symmetrical versatility is possible in that the positions of the active beads can be changed to produce an isodose distribution specific to the geometry of the individual tumor beds. What does that mean?

A That means in the treatment planning phase of this treatment, when you put in dummy sources to image, you look for the best distribution of active sources and inactive beads, these are spheres, active and inactive spheres, so that the isodose distribution conforms in three dimensions, as closely as possible to the shape of the, in this case, they call it a tumor bed, it's the cavity.

Q Does the specific geometry of individual tumor beds vary patient-by-patient?

A Yes.

Q And it does so even after the balloon is inflated; isn't that right?

A Are you saying that when the balloon is inflated that the geometry of the balloon changes over the next 48 hours?

Q No. You told me earlier that you believed that in the Ashpole device the balloon was inflated to conform the tissue to the shape of the balloon; right, do you remember that?

A The balloon will conform to the natural shape that the cavity allows it to go to, which will be roughly spherical, maybe elongated somewhat, but fairly uniform, rather than the normal cavity, which has many bumps and crooks and crannies in it, it will make it a fairly uniform structure.

Q Is it fair to say that the difference in the shape of the cavity wall and the inflated balloon, once it's implanted and inflated, is not a significant difference as the -- the cavity wall significantly conforms to the shape of the balloon?

A Ashpole doesn't discuss this, he doesn't discuss if there are pockets of blood or pockets of air that are stuck between the two, he doesn't go into those details.

can be moved within the volume of the outer balloon, but it -- but I would interpret it to mean that the surgeon has the opportunity to do this.
Q This statement, here, isn't necessarily referring to the balloon, is it, it just says --
A It's talking about the -- the -- it's talking about the device, in general.
Q But it's not necessarily referring to the balloon, is it, the inner balloon?
A It -- it's not only referring to the inner balloon, that is correct.
Q It's not necessarily referring to all components of the balloon, is it, it just says, modular assembly of components?
A It says the components are assembled, the components. I've -- I would interpret that as meaning the important components that are being assembled.
Q Which line are you reading from?
A I'm reading, in some embodiments, the inventive devices are divided in pre-assembled form. The components are assembled in advance. In certain embodiments the inventive devices are configured to

permit modular assembly of components.
Since this is the sentence after the previous sentence I would think they're talking about the components that, in some embodiments, are pre-assembled and in some embodiments are not pre-assembled and are modular.
Q If we look back at figure three, let's assume that we're talking about an embodiment where the inner balloon is fixed inside the outer balloon, for the purposes of this discussion, okay?
If that were the case isn't it true that there are certain prescribed isodose shapes that could not be treated with this device?
MR. MAURER: Objection to form.
THE WITNESS: Can you clarify that?
BY MR. COHN:
Q Well, if -- if the position of the inner balloon is fixed inside the outer balloon then there may be some prescribed isodose shapes that can't be treated with this balloon?
MR. MAURER: Objection.
BY MR. COHN:

Q Is that right?
MR. MAURER: Objection to form.
THE WITNESS: Do you want to rephrase that?
MR. COHN: Sure.
BY MR. COHN:
Q If the inner balloon in figure three is fixed within the outer balloon then the shape of the isodose delivered by that device would be fixed; wouldn't it?
A The shape of the isodose distribution depends on the shape, size, and size, of the inner balloon. And it doesn't matter whether the inner balloon is fixed or not. It's defined by the shape and size of the inner balloon.
Q If the -- if the location, shape and size of the inner balloon is fixed then the -- the shape of the isodose from that device would be fixed; correct?
A Yes.
MR. COHN: Let's take a short break.
MR. MAURER: Okay.
THE VIDEOGRAPHER: Going off the record, the time is 3:16 P.M.

(Recess.)
THE VIDEOGRAPHER: Back on record, the time is 3:25 P.M.
BY MR. COHN:
Q Just another question or two, Doctor. If I had a device like in figure three that we discussed where we'll assume that the inner volume is fixed in terms of location, size and shape, okay? And you told me that the isodose curve from that would be of a fixed shape; do you remember that?
A Yes.
Q Okay. If I -- I -- if you were prescribed by a physician to deliver an isodose that had a different shape than the shape that could be delivered by our assumed device would you be able to deliver that isodose with that device?
A If this balloon is fixed?
Q Correct.
A If the balloon is fixed then it would not be possible to change the shape because it's filled uniformly with a radioactive material.
MR. COHN: Okay. I pass the witness.

MR. MAURER: I've got one or maybe two follow-up questions.

EXAMINATION BY COUNSEL FOR DEFENDANT SENORX

BY MR. MAURER:

Q Will you pull up, Dr. Orton, pull up the article by Dr. Ashpole, which is Exhibit 2. Do you have that in front of you?

A Yes.

Q And do you recall, during the questioning by Mr. Cohn about this exhibit, he asked you about what are -- what are the factors that go into a dose that exceeds the maximum permissible dose, and you said, there are a number of factors, including volume, dose rate, fractionation, and maybe one or two other things; do you remember that line of questioning?

A Yes.

Q All right. Why is fractionation important or why is that a factor in determining what is a dose that is permissible or not permissible?

A There are many things to be taken into account, there. The -- the main reason why we fractionate brachytherapy is to get the maximum

difference between the bad effects that occur in tumor cells and the bad effects that occur in normal cells.

We want to not kill too many normal cells, so as to exceed the tolerance of those normal tissues that the cells are in, but we need to go to a high enough dose to kill all of the tumor cells if we're looking to cure the patient.

And the reason that fractionation works to do that is that normal cells are better able they're more capable of repairing radiation damage than are tumor cells.

And so we have to take that advantage to the maximum benefit. And what we do is we fractionate, which means we give a little bit of radiation, and then give time for the normal cells to repair and, incidentally, the tumor cells to repair the damage.

But the normal cells do it better than the tumor cells, so we've got a bit of an advantage there, then repeat that with a second, third, fourth, etcetera. So each fraction gives you a bigger and bigger advantage in killing cells between the normal

cells and the tumor cells.

Q Does -- I'm sorry, are you finished?

A I can go a little bit further.

Q It's your answer, I want you to answer it completely.

A In -- in Ashpole there's another factor, and that's dose rate, with a high dose rate in load afterloader during the fraction of treatment the fraction is given so quickly that there isn't any opportunity for these normal cells to repair. So you don't get an advantage during that fraction.

Whereas, Ashpole irradiates at 250 centigrade per hour. And that's slow enough that there is difference in the repair during the treatment.

The treatments are typically three or four hours. During that treatment at 250 centigrade per hour there's sufficient opportunity for the normal cells to repair better than the tumor cells.

So it makes a difference the rate at which you give the fraction and the time that you give and the number of fractions you give to allow that repair

to take place.

Q Does Dr. Ashpole --

THE VIDEOGRAPHER: Excuse me, blackberry interference, missed the question.

BY MR. MAURER:

Q Does Dr. Ashpole describe a fractionated or unfractionated method of treatment in his article?

A He describes a fractionated treatment. Treatments typically last three to four hours. And interpreting exactly what he says, he doesn't say how many fractions he used, but if you interpret the numbers here it looks like he uses four or five fractions.

MR. MAURER: I have no further questions.

MR. COHN: I have a couple.

EXAMINATION BY COUNSEL FOR PLAINTIFF HOLOGIC/CYTYC

BY MR. COHN:

Q Have you ever applied a dose of greater than 60 Gy to a patient receiving brachytherapy?

A Again, you're using the wrong terminology. I don't apply. The people who give the radiation to the patient apply and the physician prescribes. I do

the calculations behind the scenes.
Q Okay.
A So I don't put radiation into a patient, personally.
Q Do you recall ever calculating a dose for a patient where more than 60 Gy would be applied?
MR. MAURER: I -- I object as this is beyond the scope of the cross.
A May I answer the question, anyway?
Q Yes.
A Many, many times, many cancers require a lot more, especially gliomas, require -- they're very resistant to radiation treatment -- and they require a lot more. And, in fact, on one occasion we gave over 100 Gy to a patient's brain to treat a very resistant cancer in the brain.
So you could go to much higher doses in certain tissues, and certain tumors require you to go to much higher doses to cure them.
Q Was there any necrosis of normal brain tissue in that hundred Gy dose that you're thinking of?

A We don't know, this was -- this was -- I never saw the follow-up on this patient.
Q Okay, last question. Sitting here today do you have an expert opinion as to whether a dose above 65 Gy to brain tissue is or is not lethal to normal brain tissue?
A Again, it depends on the freight, it depends on fractionation, it depends on the volume of the brain that you're irradiating, all these factors that we've discussed before, it's very dependent on all of those factors, for example, with a gamma knife we treat brain tissue with enormously high doses, but a tiny little volume of tissue gets irradiated. And, therefore, we can go to much higher doses without damaging the normal brain tissue. So it's a volume effect as well as a dose rate and fractionation effect.
Q What does Ashpole mean when he talks on the front page about, quote, the limited tolerance of normal brain has restricted the maximum permissible dose to about 55 to 60 Gy?
A Again, I -- I didn't write the paper, so I

can't tell you what he means, but I can interpret what I think he means.
Q Right.
A And what I think he's referring to, here, I think he's primarily referring to volume of tissue that's irradiated.
When you do an interstitial implant or any other kind of treatment of brain you often irradiate a lot more normal brain than you need to in order to irradiate the tumor bed.
The difference here is that you're putting the radiation inside the tumor bed, irradiating outwards, and most of the normal brain tissue is way outside and getting much lower doses than 50 Gy.
So I think that's what he was referring to, he has come out with a device that overcomes that problem of tolerance.
MR. COHN: I have no further questions.
MR. MAURER: Okay. We're done.
THE VIDEOGRAPHER: Going off the record, this concludes today's deposition of Dr. Colin Orton. The time is 3:34 P.M.

THE REPORTER: Mr. Cohn, do you want the same order as the earlier deposition today, a rough ASCII right away and the final as soon as possible?
MR. MAURER: Yes.
MR. COHN: Yes, absolutely.
THE REPORTER: And the final yesterday?
MR. COHN: Yes.
MR. MAURER: Right.
(Signature having not been waived, the deposition of Colin Orton, Ph.D., was concluded at 3:35 P.M.)

Exhibit 34

IN THE UNITED STATES DISTRICT COURT
NORTHERN DISTRICT OF CALIFORNIA
SAN JOSE DIVISION

HOLOGIC, INC., CYTYC CORPORATION,
and HOLOGIC, L.P.,
Plaintiff,

vs. CASE NO. C08 00133 RMW

SENORX, INC.,
Defendant.

AND RELATED COUNTERCLAIMS

- - -

Videotaped Deposition of
PHILIP Z. ISRAEL, M.D.,

Taken by Marc A. Cohn,

Before Gayla Cagle,
Certified Court Reporter,
Registered Professional Reporter,

At the offices of The Breast Center,
Dr. Philip Z. Israel,
Marietta, Georgia,

On Wednesday, April 2, 2008,
Beginning at 4:39 & ending at 7:56 p.m.

- - -

DIGITAL EVIDENCE GROUP
1111 16th Street, NW Suite 410
Washington, DC 20036
(202) 232-0646

because that can be a very broad area, but certainly I probably would not.
Q Can you tell me what the circumstances -- strike that.
Can you tell me what kind of circumstances would lead you to use a product if it wasn't FDA approved?
A I can't.
Q FDA approval is defined by the labeling of the product; is that right?
MR. FORKNER: Objection to form, lack of foundation.
A I don't know what that means. I'm not familiar with the word "labeling."
Q Do you know what I mean when I say instructions?
A Instructions, yes.
Q The FDA approval -- strike that.
Do you understand that an FDA approval is a finding that the device is safe and effective for its intended use?
A Yes.

MR. FORKNER: Objection to form, lack of foundation.
Q And that "intended use" is expressed at least in the instructions; is that correct?
MR. FORKNER: Objection to form, lack of foundation.
A I guess. I mean, you know, these are pretty definitive comments, and I have no broad-based knowledge about what the FDA regulations and the labeling are. You know, in general, I don't deal within that area. I just know devices are approved or they are not.
Q Did you read the Contura Instructions For Use before you implanted it?
A What instructions?
Q The instructions that come with the product.
A Yes.
Q Do you know what I'm talking about?
A That come within the box?
Q Yes. Do you know what an IFU is?
A No.

Q Instructions for Use?
A (Witness shakes head negatively.)
Q When I say instructions, I'm referring to the instructions that come with -- that are shipped with the Contura. Do you understand what I mean by that, the product documentation?
A Yes.
Q Let's see if I can pin this down because I don't want to be misunderstanding.
A Yes.
Q When you receive a Contura from SenoRx, what's in the box?
A The product and the accessories and I think a pamphlet describing the device.
Q Describing how to use the device?
A Uses and restrictions.
Q Are you familiar with the term off-label use?
MR. FORKNER: Objection to form.
A Somewhat.
Q What's your understanding of that --

MR. FORKNER: Objection to form, lack of foundation.
Q -- term?
A My understanding is that the FDA, in approving a device, I think they make it clear that they don't want to be involved in the practice of medicine, but that they do approve certain devices for certain uses.
And I guess if there is variability in how a physician might apply or use a device, that might constitute off-label use.
Q Are you aware that the instructions that are shipped with the Contura MLB contain a warning that says, "Do not use if the skin to balloon distance is less than five millimeters"?
MR. FORKNER: Objection to form, mischaracterizes the document, and the Doctor hasn't been provided with this document to consider.
A Was I aware that this was in the FDA document?

Q Were you aware that this is in the instructions that are shipped with every Contura?
MR. FORKNER: Same objection.
A Yes.
Q And that means that the FDA has not approved the Contura for use in situations where the skin to balloon distance is less than five millimeters. Is that your understanding of what that means?
A No.
MR. FORKNER: Objection, lack of foundation.
A That's not my understanding.
MR. COHN: You've got to let him object, and then you can answer
MR. FORKNER: Objection, lack of foundation. Again, the Doctor doesn't have the warnings in front of him.
A But, no, that is not my understanding.
Q What's your understanding of such a

warning in the instructions?
MR. FORKNER: Same objection.
A Now, you asked me if I had looked at this, and I recall that it says that when a surgeon or a doctor is implanting a device, a balloon brachytherapy device, that at the time of implantation, initial implantation, the skin spacing, based on -- well, what I use is ultrasound -- should be greater than five millimeters.
And I interpret that to mean that the five millimeters relates to the implantation of a device, not to a treatment regulation.
Q I'm not sure I understand the difference.
A Well, I can only give you my interpretation. If I am contemplating implanting a catheter and I'm looking at the cavity with ultrasound, and if the skin spacing at that time is less than five millimeters, I would be reluctant to put in a catheter.

Now, if it's greater than five millimeters, I will put in a catheter.
Q The Contura?
A Yes. Yes.
Q But this does not relate to radiation treatment. What restricts -- in my mind what restricts radiation treatment is not that five millimeters, but it's safety of radiation dose to skin, which is a different issue you can have. You can have safe delivery at a more narrow spacing than five millimeters.
MR. COHN: Can we go off the record for a second?
THE VIDEOGRAPHER: Off the video record at 6:07 p.m.
(Deposition in recess, 6:07 p.m. to 6:11 p.m.)
MR. COHN: Forgive me if I'm a little out of breath. Let's mark this as Exhibit 2, if we could.
(Whereupon a document was identified as

Plaintiff's Exhibit 2.)
Q And I'm handing you -- let me read it here. The Instructions For Use for the Contura Multi-Lumen Balloon, models B-00145 and B-01145. And I will ask you if you've seen that before.
A Yes.
Q When have you seen that?
A Well, it's in the packet.
Q These are the instructions that I was referring to.
A I see.
Q If you could turn to the second page, the one without the sticker on it. At the top of the middle column, this is the sentence I was referring to. It's the second sentence in the top bullet point of the middle column. It's that middle column there.
At the very top it says: Do not use if the cavity is too small or if the skin surface to balloon surface distance of less than five millimeters will result. Do you see

that?
MR. FORKNER: Actually, on this version, it's on the first column. So just to be clear, it's on the first column in the warning section, maybe the fourth bullet point in.
THE WITNESS: Oh, it's right here.
Q I was reading the version on my computer.
A Here it is right here. Okay.
Q Can you read the sentence starting at "do not"?
A Yes. Do not use if the cavity is too small or if the skin -- if a skin surface to balloon surface distance of less than five millimeters will result.
Q Do you know why that warning is in there?
MR. FORKNER: Objection to form.
A I think it's reasonable.
Q A reasonable warning?
A And this is what we do. If the skin

spacing is less than five millimeters on my ultrasound, when I make the decision to insert the catheter, if it's less than five millimeters, I don't insert it.
Q Now, I think you said in your declaration that you've implanted a Contura where there was a two-millimeter skin bridge; is that right?
MR. FORKNER: Objection to form, mischaracterizes the declaration.
A It was not two millimeters when I put the catheter in. It was, I think, 5.4 millimeters when I put the catheter in.
Q And it's your interpretation of this warning in the IFU that that refers only to the skin thickness before inflation of the balloon?
A Even after inflation of the balloon, it was 5.4.
Q How did it become two, then?
A Oh, this is a problem that we -- this is one of the major issues that we have to deal with, and that's why the multi-lumen has

turned out to be such a positive device.
I think two reasons. One is that when we measure with the -- measure the distance with ultrasound, it is not quite as accurate as measuring it with CT. So after we put -- all right. That's one reason.
And the other is that we initially inflate the balloon. We do our reading. We dress the catheter in the wound, and we send the patient to radiation oncology.
The time lapse, I think, with additional time -- it may be an hour before they do their CT. This compression apparently continues to develop, to change. So my 5.4 can become 4.4 or 3.4 or even two millimeters by the time they do their CT. I don't keep the patient here an extended period of time. I have to send them on over.
Now, they do the final readout. And if the final readout is two millimeters, which it was in one case that I had, then, of course, they look at dose delivery with the multi-lumen

approach and determine if they can deliver a safe amount of radiation to the skin. And in this particular case, their determination was they could do it safely, and they proceeded.
Q Have you seen any clinical data showing that the Contura MLB can be used to treat tissue with a skin distance of less than five millimeters?
MR. FORKNER: Objection to form.
A We are -- we know, the physicists know, what a safe radiation dose to the skin is. Using the multi-lumen device, they can show precisely the amount of radiation the skin will receive.
And if you are only using a central lumen, you cannot vary that, of course, but using an offset lumen, you can precisely. I mean, I talked to the physicist about this particular case.
I said, you are going to treat a two-millimeter lumen?
He says, don't worry. It's fine.

with patients to ensure -- to look at cosmesis and other things like that?
A Yes.
Q And who performs that follow-up?
A I do.
Q Have you followed up with the two patients of yours that were treated with less than five-millimeter skin distance?
A I have.
Q And have you noticed anything -- how is the cosmesis on follow-up?
A The cosmesis is excellent on both of those. I have not -- in fact, I saw both those patients -- this week I saw the first one we did, and she looked great. And then the lady who had the two-millimeter, I saw her within less than two weeks, and she is out probably eight months now, seven or eight months. She looked fine. We are not having -- you know, there have been issues about seroma formation, painful seromas, scarring, skin changes, and we have not noted that.

Q Other than providing a dangerous dose of radiation to the skin, are there any other risks that are posed by having a skin distance less than five millimeters that you are aware of?
A Not that I'm aware of. It's usually a tissue reaction that can be severe, can be minimal, that effects the integrity of the skin and the cosmetic appearance of the skin.
Q Is this related to the restriction of blood flow in the skin because the tissue is so thin there?
MR. FORKNER: Objection to form.
A Well, I think that it's more than that. We know that when the balloon is too close to the skin, the recommended radiation dose is exceeded, and that's going to cause a direct harm to the tissue simply because of radiation, not necessarily because of blood supply. Blood supply may be, you know, an issue.
And then, of course, another issue

is whether or not the patient gets certain types of chemotherapy that can produce a condition called radiation recall.
Q What's radiation recall?
A It's a reaction of the skin to the radiation, which is exaggerated by the administration of chemotherapy. And it's difficult to predict. It doesn't occur every time.
Q Do you believe that risk would be increased if the skin distance was -- with reducing skin distance?
MR. FORKNER: Objection to form.
A We know that. Yes, that does seem to be the case. As is talked about at practically all the meetings, it is recommended that if the patient is going to get Adriamycin, that if they have a thicker skin spacing, they are going to have less reaction.
Q Do you know whether any of the patients that we discussed that were treated with a skin distance of less than five

millimeters have undergone the Adriamycin treatment you mentioned?
A I don't think they did.
Q Have you seen any data to show that a skin distance of less than five millimeters is safe for patients undergoing Adriamycin?
MR. FORKNER: Objection to form.
A We don't have definitive data on that. We do know that -- or we seem to know, I think there is a consensus of opinion that the wider the skin bridge in patients that are going to get Adriamycin, the less chance that they will have to experience recall reaction. But that's with all, you know, that's with all the devices. There is no difference between Xoft, MammoSite, Contura, except for the ability to make it a wider skin spacing.
Q Other than a risk posed by radiation to the skin, are there other risks that are presented by having a skin distance of less than five millimeters that you are aware of?
A Well, yes, there is one major one.

Q Which is?
A The catheter has to be pulled, and then the patient has to undergo whole breast radiation.
Q And the catheter would have to be pulled because --
A Of narrow skin spacing. So that's, you know, an additional problem. In other words, if you go ahead and treat, you are going to get skin damage; and if you don't treat, you are going to pull the catheter, so either way you've got a problem.
Q What I'm trying to get at is if you treat and the skin distance is too narrow, you could overexpose the skin to radiation?
A Right.
Q Other than that overexposure to radiation, are there other risks that are presented by having a narrow skin distance? For example, is there a risk that the skin ruptures because it's so thin? Is that possible?

A Oh, yes.
MR. FORKNER: Object to the form.
Q That is possible?
A Yes. Certainly you can get varying degrees of reaction all the way from just a simple sunburn-type reaction in the skin, to blistering in the skin, to frank necrosis of the skin where the skin sloughs out and leaves a large hole looking down into the lumpectomy cavity. All of those are possible if the skin dose is exceeded.
Q Well, again, I'm not trying to talk about the skin dose. Let's think of it this way. If I put in a Contura, a balloon, and I inflate it and I find that the skin distance is less than five millimeters, without applying any radiation, no radiation is applied, and the patient is walking around for a week or two, let's say, with the balloon inflated and the only two-millimeter skin distance at the surface, are there risks posed to the skin due to its being only two millimeters versus five

in that instance?
A We have not noted that. However, the cases are limited in number. But I have not seen it. The cases where we have had under five millimeters have done just as well as those with ten millimeters. I've not noticed any difference. This is something we will have to look at, continue to look at, as we acquire more cases.
Q It could be a risk?
MR. FORKNER: Object to the form.
A It's been discussed, but we have not -- it's a theoretical possibility. It seems to be logical, but we have not seen that.
Q I'm sorry. What is the risk that's being discussed?
A That a narrow skin bridge might interfere with blood flow.
Q That could result in necrosis?
A It could, but we haven't seen it.
Q What else could it result in?
A I don't know. Skin reaction, you

know, here again, I guess it could be -- even that, a little bit of ischemia could result in blistering or a full thickness skin loss or tissue necrosis, although we have not seen it. But we don't have that many cases, you know. I mean, we've not seen it, though.
Q I understand. Besides the ischemia caused by blood loss --
A Not by blood loss but by --
Q I'm sorry. Restriction.
A -- compression.
Q I keep talking over you, and I apologize.
A And I talk over you, and I apologize.
Q The compression of the skin causes restriction of blood flow?
A Compression of the tissue underlying the skin and the skin, mainly underlying it.
Q Could the thinness of the skin cause the -- is there a risk that the skin could rupture because it's thinner than five

millimeters?
A You mean the suture line rupturing?
Q No. The skin bridge itself because it's less than five millimeters.
MR. FORKNER: Objection to form.
A I'm sorry. I spoke too soon.
Q Go ahead.
A Anything is possible. We have not seen it.
Q There has been no clinical study done of the risks presented by a balloon with a skin bridge less than five millimeters.
MR. FORKNER: Objection to form.
A How many have we treated countrywide? Not that many. But so far we have not seen that happen. It's something we will be looking at as we go forward.
Q But other than restricting the blood supply and then potential rupture of the skin bridge, are there other risks that you can think of to the skin bridge of less than five millimeters, other than radiation?

MR. FORKNER: Objection to form, has a false predicate. Go ahead.
A I can't think of any.
Q There could be others that are unforeseen?
A "Could be" is -- you know, I guess anything is possible, but I've not heard anything else discussed or -- and I can't think of anything that would be a reasonable issue to put on the table.
Q And without data, we wouldn't really know at this point; is that right?
MR. FORKNER: Objection to form.
A We don't have enough data for any -- no.
Q This should be my last line of questioning. Has SenoRx ever told you -- strike that.
Have you ever heard SenoRx -- have you had any discussions with SenoRx or SenoRx personnel about treating patients with less than a five-millimeter skin bridge?

A I'm not sure what you are asking me. Of course, when we treated these few patients that did fine, there was lots of chatter and interest in these patients.
So, yes, there has been a lot of discussion about these narrower skin bridges that have been, at least to this point, successfully treated.
Q Have you given SenoRx any documents or PowerPoint slides or anything written regarding patients that you've treated with less than a five-millimeter skin bridge?
A They probably have my presentations at the meetings because I downloaded that onto their computers. You may have it too. I don't know. But other than that, have I given, no, I haven't given them anything.
Q Are you aware of whether SenoRx has disseminated the presentations that you've given at the meetings to other doctors who weren't at the meetings?
MR. FORKNER: Objection to form.

A I'm not aware that that has happened.
Q You are not aware one way or the other?
A One way or the other, no. They certainly haven't asked me for permission to do that.
Q Do you believe that such permission would be necessary --
MR. FORKNER: Objection to form.
Q -- for them to do that?
A I don't know. Because I didn't tell them they couldn't do it because it never came up. But, you know, all of these companies have used my material.
The first case I did for MammoSite was probably shown hundreds, if not thousands, of times around the country and around the world. And actually, nobody ever asked me permission for that. But they used it for years because it was a great video clip. And Xoft has used some of my clips.

Q So let me see if I can understand that.

For the purpose of understanding those terms in a regulatory context, do you consider yourself as an expert on speaking to those issues?

A No.

Q When you use the terms safe and effective, what do you generally mean by those terms?

A Well, safety meaning that it's not going to harm the patient if used properly. And effectiveness, as long as the device delivers the same amount of radiation to the same targeted tissue, that MammoSite or Xoft or any of the other partial breast radiation devices, as long as they deliver the same amount of radiation to the same target tissue, I think that it's going to be equally effective.

MR. FORKNER: We have to change the tape.

THE VIDEOGRAPHER: Give me one minute. End of tape number two, off the video record at 7:34 p.m.

(Deposition in recess, 7:34 p.m. to 7:36 p.m.)

THE VIDEOGRAPHER: This is the beginning of tape number three, back on the video record at 7:36 p.m.)

Q Doctor, you were asked a series of questions during the course of the deposition about potential risks of the use of a brachytherapy device with a skin bridge of less than five millimeters. Do you recall that line of questioning?

A Yes.

Q And you identified a few possible risks; correct?

A Yes.

Q Are you able to quantify those risks, say, how likely they are to happen of those various potential issues?

A Well, I would say to some extent we

can predict as long as we keep the dose to skin down to a recognized, acceptable level, we have not zero complications but very few serious complications and not many minor complications. I think it's almost all dose related.

Q Okay. You were talking about a particular risk about Andriamycin, if I said that right?

A Yes. Adriamycin.

Q Sorry.

A Adriamycin is a chemotherapeutic agent.

Q And for that particular risk, is that the same answer?

MR. COHN: Objection to form.

A In that -- what we do to minimize the reaction of recall is that we want to have as wide a skin bridge as possible, and we want to delay the initiation of chemotherapy for three weeks after the radiation is finished.

Q So when treating a patient with a

skin bridge of less than five millimeters, are there steps you can take to minimize the risk of a reaction on a patient who is taking that drug?

MR. COHN: Objection to form.

A Using which catheter? Any of them?

Q Well, let's start with any of them.

A Well, of course, we can't diminish the dose to the skin with the central lumen, but with a multi-lumen device, we can effectively reduce the level of radiation to the skin which will help us diminish the probability of any kind of reaction with chemotherapy, and that's an important issue.

Q I think you indicated that you were, if not the first, one of the first physicians to implant the MammoSite device; is that correct?

A Yes.

Q What clinical testing of that device existed to your knowledge prior to your implantation of that device?

A We had no data. We had FDA approval to safety and efficacy, but we had no data to rely on. And, you know, with new techniques like this, if you wait for data, you will never do anything new. You accumulate data as you go along.
Q And at the time that you implanted the MammoSite device without clinical data, were there risks, possible risks to such implantation?
A There were. Let me elaborate for just one minute, you know. We did have some data based on interstitial brachytherapy, which has not come up tonight, and that's not a balloon brachytherapy, but it still is brachytherapy, and we did have some data there.
But we had no data with balloon brachytherapy, but we thought it was safe. The FDA thought it was safe. The interstitial brachytherapy had been safe, and we found out that it is safe, but we didn't know it

initially.
Q Have you ever used the MammoSite device in a manner that wasn't indicated in the label? Obviously, you don't have the label in front of you, but to the extent you can remember.
MR. COHN: Objection to form.
A Well, we have tried not to use MammoSite in cases where there is a thin skin bridge, below seven millimeters. And when the radiation physicist does any dose planning with a narrow skin bridge with a MammoSite, they have no options. They have no way to reduce the skin dose. So we don't proceed.
Q And have you ever used the MammoSite device with a skin bridge distance of less than seven millimeters?
A You know, I can't tell you 100 percent, but we try not to. Now, you know, we've done hundreds, and to my knowledge, to my recollection, no, but there may have been a six millimeter or a five millimeter and under

certain dire circumstances that were used in patients where whole breast radiation would have been a disaster such as in some very large breasts, but to my recollection, no.
Q You were talking earlier about how as a surgeon you are able to discuss the potential benefits of a balloon brachytherapy device to ribs or some of the other human structures. If you could just elaborate on the risk to ribs in conjunction with the use of brachytherapy devices.
A Initially, we minimize the issue of excessive dose to rib with the MammoSite. And I think we minimized it because we couldn't do anything about it, so we just accepted the fact that the rib may receive an excessive dose. We didn't know.
So as we have gone along, it has -- we have found out that an excessive dose to rib does cause problem. And as I stated earlier, we have documented cases of rib fracture and periosteal reaction from overexposure. So now

with the ability to tailor the dose, we are trying to protect the rib.
Q Finally, you indicated that you had created some PowerPoint slides for a presentation or a meeting, I think you indicated. What was the purpose in you creating those slides? Why did you do it?
A Like the video clips of the procedures?
Q Sure.
A So that we could share our experience and our information with other doctors who want to use the devices. And I've done that with all three balloons, all three companies.
MR. FORKNER: I will pass the witness.
MR. COHN: I have a few more questions.
RECROSS-EXAMINATION
BY MR. COHN:
Q We were talking about safe and

effective with counsel. Isn't the point of the registry study that you are going to be a part of with SenoRx to prove the safety and effectiveness of the Contura MLB for skin thickness less than five millimeters?

MR. FORKNER: Objection to form, lack of foundation.

A Of course. We will be looking at everything with the registry. Going forward as we accumulate data, we are looking at everything. So far everything looks good. We don't know about, you know, what's going to turn up.

And that's the same reason we did the registry with the MammoSite, because we had no data, but we proceeded, and we learn as we go.

Q So it's possible that the registry study of Contura could show that it's not safe and effective for use in a skin distance of less than five millimeters?

MR. FORKNER: Objection to form,

lack of foundation.

A I will answer that by saying anything is possible. However, we know the radiation dose to the skin at two millimeters and three millimeters, and we know it calculates safe. This is a known factor. We are not flying through the clouds.

Q Well, but then why have the registry study?

A Well, you want to compare. You want to confirm. You want to see what's going to develop. The same reason we had the registry with MammoSite and the same reason that Xoft is going to have a registry.

Q For whom is the registry study for? For other doctors?

A Probably is to convince skeptics that it's okay. But you always want data. You always want to monitor what you do, with everything, you know, even new and old. We monitor everything we do.

Q And this registry study is going to

be a randomized, double-blind study, as far as you know?

A No. We haven't done any randomized brachytherapy studies, registries. We only report the data. There is no double blind. We only report data on the cases that we do. And we look at, you know, complications, try to codify them and numerically see what's a big problem and what's not a big problem.

I don't think we are going to see -- I don't think we are going to see much difference in the registry. I think the registry with MammoSite has been excellent in terms of proving safety. Efficiency, if you base efficiency on recurrence of cancer, you've got to wait 15 years.

Q You mean efficacy? You said efficiency.

A Well, tumor recurrence. We expect it to be the same, though, with all of these devices because we are delivering the same amount of radiation. We can deliver it in more

patients with the Contura and hopefully spare skin and bone, which is going to help with complications.

Q In the registry study, do you expect to be paying full price for the Contura balloons that you will be using?

MR. FORKNER: Objection to form.

A I haven't heard otherwise. And in all the registries that we've done -- well, we've only done the MammoSite, and, yes, that didn't affect the price of the balloon.

Q Will you be compensated for your work on the registry study?

A We were with -- I don't know. I suspect that we will because there is lots of data collection and paperwork that needs to be done.

Q It's a significant undertaking?

A It requires a lot of work, a lot of follow-up.

Q It's expensive, too, to conduct a registry study?

MR. FORKNER: Objection to form.
A Expensive for whoever is conducting it, and that expense rolls down to us because we have to have personnel. They are not going to send anybody down here to do this work for us. So some of our office personnel have to spend their time collecting this data, abstracting it.
Q Do you know how many doctors will be part of the SenoRx registry study?
A I don't know.
Q Do you know if it will be more than ten?
A I would expect so.
Q Do you expect it would be more than 30?
MR. FORKNER: Objection to form, lack of foundation.
A Thirty sites -- 30 -- I wouldn't be surprised.
Q Why undertake such a registry study for, you said, for some skeptics? It's more

important than that, isn't it?
MR. FORKNER: Objection to form.
A Well, data collection to prove worthiness and to review complications and to see where the complications are coming from. I think it's -- I mean, registry studies are common, and I think they are good.
Q They are important to doctors?
A Encourage doctors to do that.
Q Are they important to doctors?
MR. FORKNER: Objection to form.
A Yes.
Q I think you said that when you first started implanting MammoSites, there was no clinical data of the safety and effectiveness of the MammoSite?
A Of balloon brachytherapy?
Q Yes.
A None had ever been done.
Q And when you first started performing or implanting MammoSites, you said that was after FDA approval of the MammoSite?

A Yes.
Q It wasn't part of a study?
A No. FDA approval was in May '02, and I put my first one in in August '02. And I think the first one was done maybe a couple of months before I did mine.
Q You understand there was a study done of the MammoSite?
MR. FORKNER: Objection to form.
Q Clinical study?
A Implanting catheters in --
Q Human beings.
A -- in human beings. No. I'm not aware of it.
Q You are not aware of a clinical study that's described in the Instructions For Use of the MammoSite?
A I'm not aware of, you know, a clinical trial in patients prior to -- prior to FDA approval?
Q At any time.
MR. FORKNER: Objection to form.

A At any time. The only study that's been done, as far as I know, you know, is sponsored by the company and run by organized medicine would be the registry.
Q "The registry"?
A I'm sorry?
Q You said "the registry."
A The registry for MammoSite. It's now under the auspices of the American Society of Breast Surgeons. And I think it's been closed. We had about 1,500 cases, 1,600 cases.
Q In the year -- let's just set a date. In June of 2007, you said you implanted your first Contura?
A Yes.
Q In the year prior to that, roughly how many MammoSites did you implant?
A I would say between a low number of 50 and a high -- I'm not sure I did 100. That's a wide variation, but I haven't counted --

Exhibit 35

IN THE UNITED STATES DISTRICT COURT

FOR THE NORTHERN DISTRICT OF CALIFORNIA

HOLOGIC, INC. Plaintiff, vs. SENORX, INC. Defendant.	Case No.: CV 207-ML-01816-B

HIGHLY CONFIDENTIAL

April 4, 2008

Richmond, Virginia

The videotaped deposition of DOUGLAS W. ARTHUR, M.D., a Witness, taken at the instance of the Plaintiff, before Helen B. Yarbrough, RPR, CCR, a Notary Public for the State of Virginia at Large, beginning at 8:19 a.m., at Virginia Commonwealth University, Medical College of Virginia, 401 College Street, Richmond, Virginia; said deposition taken pursuant to the Federal Rules of Civil Procedure.

DIGITAL EVIDENCE GROUP
1111 16th Street, NW Suite 410
Washington, DC 20036
(202) 232-0646

some adjustments in what you're doing to make sure it's safe if you're close to these kind of warning things. I don't know if I've clearly stated that, but . . .

Q Let's look at -- if you go to the fourth bullet point under the "Warning" section --

A Uh-huh.

Q -- it reads, "The breast cavity must be imaged before implantation to ensure the applicator will fit appropriately. Do not use if the cavity is too small or if a skin surface to balloon surface distance of less than 5 mm will result," "mm" being millimeters.

A Sure.

Q What does that mean to you?

A Well, you know, my interpretation of this is -- is that this is referring to the time of applicator placement, because obviously you are imaging it right before implantation. It's giving the surgeon or the radiation oncology some basic information to say that, you know, if -- what to anticipate after you place the -- you're trying to

think ahead in terms of what the applicator will look like once it's already been placed, and just for general guidance.

Q Okay. So let's focus on the part that says, (Transcribed as read.) "Do not use if the cavity is too small or if the skin surface to balloon surface distance of less than 5 millimeters will result."

What happens if the skin surface to balloon surface distance is less than 5 millimeters?

MR. FORKNER: Objection to form.

A Well, that -- that depends on a lot of things. I don't know that -- it depends on the device that you're using and depends on exactly where that distance might be in relationship to the device.

As -- as you and I spoke earlier in terms of the criteria that we use in appropriateness for treatment and designing, we focus on the skin dose because as we also said earlier, it's the dose that makes the difference in regards to tumor control and toxicity.

So what does that mean? You know, certainly as the -- as the skin thickness decreases, the issue

of skin dose becomes more prominent, and it's -- to be honest with you, I -- I -- you know, when I evaluate a patient to place a cavity, what I'm trying to do is anticipate what it's going to look like before I put it in. It's an expensive catheter kit, both the MammoSite and the Contura. I don't want to open one up and find out that it was inappropriately placed and I can't use it.

Q You mentioned that at small -- lesser balloon to skin surface ranges, the issue of the skin dose becomes more prominent.

A Correct.

Q What do you mean by that?

A Well, our dose -- our target is 1 centimeter from balloon surface. So our dose, the intention is to deliver our dose to 1 centimeter from the balloon surface. And knowing that anything inside that 1 centimeter is going to be hotter, we have to pay attention to the doses within that range.

The -- with a single lumen device, you -- your dose around the balloon is fixed. There's some minimal manipulation you can do, so it's not fixed

hard rigid, but it's fixed, so that the relationship between target coverage and high-dose regions is direct relational for the most part. If I'm using a single lumen device, then it's coupled with the direct location of where these structures are in relationship to the balloon.

If I am using a multilumen balloon, then I have the ability to manipulate that dose and decrease the dose to surrounding structures or increase them, depending on what's necessary. When I'm placing a balloon personally, I'm looking at how best to place that balloon to take full abilities of the catheter itself to achieve the dosimetric coverage that I want to achieve.

In its standard use, the MammoSite device is placed -- when I say "standard," I mean majority of people and my understanding of what the majority of people do is that they -- it is placed by a surgeon. It's then evaluated by the radiation oncologist as it comes in the door. In other words, the surgeon just places it out how best to put it in, not necessarily paying attention to what dosimetric needs are of the

radiation oncologist, and the radiation oncologist does their planning and decides whether they can or can't treat based on what they do.

With a single lumen, there's limited dose modification that you can use to personalize or individualize the treatment for that particular patient's needs. So it becomes a minimal modification. If you can't help -- if you can't fix it, then you remove the device.

In our hands, if we're using the MammoSite device, we also take into consideration the direction that we're placing the balloon. And I couldn't give you the number of cases, but on some cases it was appropriate for us to place the balloon in a perpendicular fashion to the skin surface so that I could take advantage of the location of the single lumen so I could drop the dose to the skin and assure that we decreased toxicity, which I would do in any case with a MammoSite balloon when it's close to 5 millimeters, because of that increased toxicity that's been shown in clinical trials.

With the Contura balloon, our abilities are

greatly enhanced in terms of moving that dose, and so, you know, the skin distance, quite frankly, is not the issue; it's what I can achieve with the skin dose.

Q Let me back up just a second. You said something before. This warning that talks about not using the -- if the cavity -- if the skin surface to balloon surface is less than 5 millimeters. You mentioned that that's for imaging?

MR. FORKNER: Objection to form.

A I'm not sure that's what I said.

Q Let me -- let's strike that. Let me just ask a different question.

A Sure.

Q Do you read this instruction as instructing you to -- the wires are tangled up.

Do you read this instruction as telling you not to -- not to use the multilumen device if, while you're using it, your skin distance is less than 5 millimeters?

MR. FORKNER: Objection to form.

A No.

Q Why not?

A I think that because -- because of the imaging phrase in this, which is why I brought up imaging prior, this is clearly focusing on the placement of the device and giving some guidance regarding -- in relationship to the skin thickness for placement of the device, and the actual use of the device is -- is not -- not part of this.

Q Help me understand why that makes sense.

A Okay.

Q If you're concerned about where that balloon is with relation to skin when you're implanting it and you're told that it can't be closer than 5 millimeters, then when you go to use it, you don't care about what that distance is, why do you suddenly not care if it was such a big point beforehand?

MR. FORKNER: Objection to form.

A "Caring's" the wrong word in terms of this. What I'm focusing on is that dose to the skin. That dose to the skin can be any measurement that you want -- excuse me -- the thickness of the skin can be any thickness that you want. I'm concerned about the dose to the skin. In a multicatheter implant, I'm

worried about dose to the skin. I can put my catheters right underneath the skin and have -- I'm worried about dose to the skin.

In a -- in a SAVI device produced by Ciena, they have published abstracts and presentations that they're talking about dose to skin. Skin thickness is not an issue unless you're unable to control the dose to the skin, such as in the MammoSite, where the dose is directly related to the skin thickness.

But ultimately, not to be redundant, my outcome from radiation treatment is directly related to the dose delivery and how it's delivered. My skin thickness can be a centimeter, and I can take a MammoSite and I can severely hurt that skin if I don't deliver the dose appropriately.

Q Okay. But -- so I guess -- I guess I had more focus on the opposite. Why do you care what the skin distance is when you're implanting it?

MR. FORKNER: Objection to form.

A I think that because -- you don't know what the skin thickness is going to be until it's implanted and the balloon's inflated. Despite commentary from

c2fb0f81-e90d-49bc-bbd7-25766da39378

people, the preplacement evaluation is a guess at what you might get. With the compression and the stretching of the skin and the surrounding tissues with the balloon inflation, which is very unpredictable from patient to patient depending on size of the breast, the density of the breast, those kind of things, and so it's not anticipated, I don't know what I can achieve with my dose until the balloon is placed, until I've done my CT scan and I've done all my contouring and done an appropriate evaluation.

To have somebody that has a small skin bridge clearly identified that stretches over a wide -- prior to placement, sets you up for a possible situation where you will not be able to achieve your dosimetric goals. And I think that was the spirit of the warning in terms of trying to avoid cases where the radiation oncologist will not be able to achieve the situation; but again, you don't know until it's placed.

So again, I -- I think this is a warning. I don't think this says that it should -- that it can not be used. It just says that, hey, if it's less

than 5 millimeters, you might have a problem, but you don't know until it's in.

Q Let me ask you a little bit about the sequence of events here. Someone comes to your office. You diagnose them with cancer. They go to have the tumor removed, and you implant one of these devices, the MammoSite or the Contura. At that point do you inflate the balloon at that point, or is it inflated later?

A It depends on who's placing it. If -- I would say the majority of placements are done by the surgeon in their office; and yes, the balloon is inflated, be it the Contura or the MammoSite, at the time of placement, and then they come to the radiation oncologist for CT scan evaluation and implanting.

At that time the balloon inflation can be changed. We can inflate or deflate depending on what we need to achieve. I've actually sometimes deflated and rearranged the orientation of the balloons, be it the Contura or the MammoSite, more appropriately and then reinflate it so I can, again, achieve my dosimetric goals.

Q Are you reimaging at that point in time --

A Absolutely.

Q -- so that you know how to rearrange it?

A When they come down, I CT scan them, evaluate it. If I need some adjustments, we adjust it and then re-evaluate it.

Q And then the patient heads off to treatment immediately?

A No. No. They go through a treatment planning process, you know, half a day depending on the physicist's schedule and getting to things. By the time you get the contouring done, the planning done, the documentation done, and then appropriately placed into the treatment delivery system -- it's all computerized and with quality assurance checks and so forth. It takes us about a half a day to get ready, and then we're ready to start. So it's not uncommon for us to do our treatment planning, scan on the morning of one day, and then start the following day.

Q Can the catheter and attached balloon move during the time before you actually begin treatment?

A How do you mean "move"?

Q Well, you spent a lot of time, and it sounds like that you spend a lot of time imaging it and figuring out exactly the position you want the balloon to, and then the patient goes home.

A Yes.

Q And you have external ports to this device that you can presumably inflate and insert radiation surfaces?

A Correct.

Q So my question is, if the patient does something while not in your clinical setting, can that balloon actually be dislodged or moved to different positions, and when they come for treatment the next day, it's not really where it was when you imaged it the day before?

A Sure. Yes, although any movements would not be as dramatic as you sort of indicate in your verbiage, but it is standard of care to do a couple things prior to each treatment. One is to position the patient exactly as they were planned. Just as simple as having the arm up or down can make a difference in the dosimetric. Sitting or lying can

Exhibit 38

#7/A

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s):	Rance A. Winkler et al.	
Application No:	09/293,524	Group Art Unit: 3736
Filing Date:	April 15, 1999	Examiner: J. Lacyk
Entitled:	INTERSTITIAL BRACHYTHERAPY APPARATUS AND METHOD FOR TREATMENT OF PROLIFERATIVE TISSUE DISEASES	
Atty. Docket No:	101360-15 (ONE-008)	

Certificate of Mailing (37 C.F.R. 1.8(a))

I hereby certify that this correspondence is being deposited with the United States Postal Service Post Office as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231 on the date set forth below.

December 20, 2000 — Date of Signature and Mail Deposit

By: Ronald E. Cahill, Reg. No: 38,403

AMENDMENT AND RESPONSE

Assistant Commissioner for Patents
Washington, DC 20231

Dear Sir:

In response to the Office Action dated June 20, 2000, please amend the above-referenced patent application as follows:

In the claims

Please amend the claims as follows:

A

Application No: 09/293,524
Group Art Unit: 3736
Examiner: J. Lacyk
Atty Docket No: 101360-15 (ONE-008)

CLAIMS

1. (Amended) An interstitial brachytherapy apparatus for delivering radioactive emissions to an internal body location comprising:

(a) a catheter body member having a proximal end and distal end;

(b) an inner spatial volume disposed proximate to the distal end of the catheter body member;

(c) an outer spatial volume defined by an expandable surface element disposed proximate to the distal end of the body member in a surrounding relation to the inner spatial volume; and

(d) a radiation source disposed in the inner spatial volume and generating a three-dimensional isodose profile that is substantially similar in shape to the expandable surface element.

A1

2. (Amended) The apparatus of claim 1, wherein the inner and outer spatial volumes are configured to provide a minimum prescribed absorbed dose for delivering therapeutic effects to a target tissue [that may include cancer cells], the target tissue being defined between the outer spatial volume expandable surface and a minimum distance outward from the outer spatial volume expandable surface, the apparatus providing a controlled dose at the outer spatial volume expandable surface to reduce or prevent necrosis in healthy tissue proximate to the expandable surface.

4. (Amended) The apparatus of claim 3, wherein the expandable surface element is adapted to contact [contacts] tissue surrounding a resected cavity and adapted to conform [conforms] the tissue to the desired shape of the expandable surface element.

A2

Application No: 09/293,524
Group Art Unit: 3736
Examiner: J. Lacyk
Atty Docket No: 101360-15 (ONE-008)

Please cancel claims 5 and 6.

~~17.~~ (Amended) The apparatus of claim ~~13~~ 16, wherein [the] a burst strength of the distensible chamber defining the outer spatial volume is greater than [the] a burst strength of the chamber defining the inner spatial volume.

~~21.~~ (Amended) A method for treating a proliferating tissue disease using interstitial brachytherapy at an internal body location comprising:

(a) surgically creating access to the proliferating tissue in a patient;

(b) surgically resecting at least a portion of the proliferating tissue to create a resection cavity within body tissue;

(c) providing an interstitial brachytherapy apparatus for delivering radioactive emissions comprising:

(i) a catheter body member having a proximal end and distal end;

(ii) an inner spatial volume disposed proximate to the distal end of the catheter body member;

(iii) an outer spatial volume defined by an expandable surface element disposed proximate to the distal end of the body member in a surrounding relation to the inner spatial volume; and

(iv) a radiation source disposed in the inner spatial volume and generating a three-dimensional isodose profile that is substantially similar in shape to the expandable surface element;

(d) intraoperatively placing the interstitial brachytherapy apparatus into the resection cavity until a prescribed absorbed dose has been delivered to tissue surrounding the apparatus; and

(e) removing the interstitial brachytherapy apparatus.

20 ~~22.~~ (Amended) The method of claim ~~21~~ 19, further including placing [wherein] the radioactive source [is placed] into the interstitial brachytherapy apparatus after the step of placing [placement of] the apparatus into the tumor resection cavity.

21 ~~23.~~ (Amended) The method of claim ~~21~~ 19, further including removing [wherein] the radioactive source [is removed] from the interstitial brachytherapy apparatus before the step of removing [removal of] the apparatus.

22 ~~24.~~ (Amended) The method of claim ~~21~~ 19, wherein the proliferating tissue is [resected from] a patient's brain.

AM 23 ~~25.~~ (Amended) The method of claim ~~21~~ 19, wherein the proliferating tissue is [resected from] a patient's breast.

24 ~~26.~~ (Amended) The method of claim ~~21~~ 19, further including configuring [wherein] the inner and outer spatial volumes [are configured] to provide a minimum prescribed absorbed dose for delivering therapeutic effects to a target tissue [that may include cancer cells], the target tissue being defined between the outer spatial volume expandable surface and a minimum distance outward from the outer spatial volume expandable surface, the apparatus providing a controlled dose at the outer spatial volume expandable surface to reduce or prevent necrosis in healthy tissue proximate to the expandable surface.

25 ~~27.~~ (Amended) The method of claim ~~26~~ 24 further including providing [wherein] a predetermined spacing [is provided] between said inner spatial volume and the expandable surface element.

Application No: 09/293,524
Group Art Unit: 3736
Examiner: J. Lacyk
Atty Docket No: 101360-15 (ONE-008)

~~28.~~ 26 (Amended) The method of claim ~~27~~ 25, wherein the expandable surface element is adapted to contact [contacts] tissue surrounding a resected cavity and adapted to conform [conforms] the tissue to the desired shape of the expandable surface element.

AM

Please cancel claims 29 and 30.

Please add the following new claims:

~~31~~ 33. The method of claim ~~26~~ 24, wherein the step of configuring the inner and outer spatial volumes includes expanding the inner and outer spatial volumes.

~~36~~ 32. A method for treating a proliferating tissue disease using interstitial brachytherapy at an internal body location comprising:

(a) surgically creating access to the proliferating tissue in a patient;

(b) surgically resecting at least a portion of the proliferating tissue to create a resection cavity within body tissue;

AS

(c) providing an interstitial brachytherapy apparatus for delivering radioactive emissions comprising:

(i) a catheter body member having a proximal end and distal end;

(ii) an inner spatial volume disposed proximate to the distal end of the catheter body member;

(iii) an outer spatial volume defined by an expandable surface element disposed proximate to the distal end of the body member in a surrounding relation to the inner spatial volume; and

(iv) a radiation source disposed in the inner spatial volume;

21

(d) intraoperatively placing the interstitial brachytherapy apparatus into the resection cavity;

(e) configuring the inner and outer spatial volumes to provide a minimum prescribed absorbed dose for delivering therapeutic effects to a target tissue, the target tissue being defined between the outer spatial volume expandable surface and a minimum distance outward from the outer spatial volume expandable surface, the apparatus providing a controlled dose at the outer spatial volume expandable surface to reduce or prevent necrosis in healthy tissue proximate to the expandable surface; and

(f) removing the interstitial brachytherapy apparatus.

33
~~37~~. The method of claim ~~36~~ 32, wherein the step of configuring the inner and outer spatial volumes includes expanding the inner and outer spatial volumes.

AS 34
~~38~~. A method for treating a proliferating tissue disease using interstitial brachytherapy at an internal body location comprising:

(a) surgically creating access to the proliferating tissue in a patient;

(b) surgically resecting at least a portion of the proliferating tissue to create a resection cavity within body tissue;

(c) providing an interstitial brachytherapy apparatus for delivering radioactive emissions comprising:

(i) a catheter body member having a proximal end and distal end;

(ii) an inner spatial volume disposed proximate to the distal end of the catheter body member;

(iii) an outer spatial volume defined by an expandable surface element disposed proximate to the distal end of the body member in a surrounding relation to the inner spatial volume; and

7-2

(iv) a radiation source disposed in the inner spatial volume;

(d) intraoperatively placing the interstitial brachytherapy apparatus into the resection cavity;

(e) adapting the expandable surface element to contact tissue surrounding the resection cavity to conform the tissue to the desired shape of the expandable surface element;

(f) delivering a prescribed absorbed dose to tissue surrounding the apparatus; and

(g) removing the interstitial brachytherapy apparatus.

35 34
~~39.~~ The method of claim ~~36~~, wherein the step of adapting the expandable surface element includes expanding the outer surface volume.

AS 36
~~40.~~ An interstitial brachytherapy apparatus for delivering radioactive emissions to an internal body location comprising:

(a) a catheter body member having a proximal end and distal end;

(b) an inner spatial volume disposed proximate to the distal end of the catheter body member;

(c) an outer spatial volume defined by an expandable surface element disposed proximate to the distal end of the body member in a surrounding relation to the inner spatial volume; and

(d) a radiation source disposed in the inner spatial volume;

wherein the inner and outer spatial volumes are configured to provide a minimum prescribed absorbed dose for delivering therapeutic effects to a target tissue, the target tissue being defined between the outer spatial volume expandable surface and a minimum distance outward from the outer spatial volume expandable surface, the apparatus providing a controlled dose at the outer spatial volume expandable surface to reduce or prevent necrosis in healthy tissue proximate to the expandable surface.

23

Application No: 09/293,524
Group Art Unit: 3736
Examiner: J. Lacyk
Atty Docket No: 101360-15 (ONE-008)

REMARKS

The above-identified patent application has been amended and reconsideration is respectfully requested. In response to the Examiner's rejections, Applicant hereby amends claims 1, 2, 4, 14, and 21-28. Claims 5, 6, 29, and 30 are canceled. Claims 35-40 are added. Claims 1 and 21, as amended, now recite that the interstitial brachytherapy apparatus comprises a radiation source disposed in the inner spatial volume that generates a three-dimensional isodose profile that is substantially similar in shape to the expandable surface element. Accordingly, claims 5, 6, 29, and 30 are canceled. New independent claim 36 incorporates all of the limitations of claims 21 and 26, while new independent claim 38 incorporates all of the limitations of claims 21 and 28. Also, new independent claim 40 incorporates all of the limitations of claims 1 and 2. New dependent claims 35 and 37 recite that the step of configuring the inner and outer spatial volumes includes expanding the inner and outer volumes, while new dependent claim 39 recites that the step of adapting the expandable surface element includes expanding the outer surface volume. Support for these limitations can be found on page 7, line 27 to page 8, line 15. Accordingly, no new matter is added by these amendments.

Response to the Indefiniteness Rejections

Claims 2, 4, 5, 14, and 22-29 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for unclear language and for lacking antecedent basis for certain limitations.

The Examiner rejects claims 2 and 26 for use of the phrase "may include" in line 3, which is alleged to render the claims indefinite. Accordingly, the phrase "that may include cancer cells" has been deleted from claims 2 and 26. In addition, claims 2 and 26 are amended to recite a "mininum *prescribed* absorbed dose" to provide proper antecedent basis for dependent claims.

Claims 4 and 28 are rejected for containing language which appears to claim a positive connection to the body. As helpfully suggested by the examiner, Applicant amends claims 4 and 28 to recite that the expandable surface element is "adapted to contact tissue surrounding a resected cavity and adapted to conform the tissue to the desired shape of the expandable surface element."

The Examiner rejects claims 5 and 29 for failing to include structure to support how the apparatus "creates absorbed isodose profiles." Applicant respectfully traverses the Examiner's indefiniteness rejections, for the following reasons. Amended claims 1 and 21 now recite that the radiation source disposed in the inner spatial volume generates a three-dimensional isodose profile. Inasmuch as claims 5 and 29 depend upon claims 1 and 21, respectively, the limitation that the radiation source generates the isodose profile should provide the sufficient structural support sought by the Examiner. Thus, Applicant respectfully argues that the structural support required for the limitations in claims 5 and 29 are present. Examiner is asked to kindly reconsider his rejections in view of amended claims 1 and 21.

Claim 14 was rejected for failing to provide antecedent basis for the limitation "the burst strength". In response, claim 14 is amended to provide antecedent basis for such limitation.

The Examiner rejects claims 22-29 for failing to recite method limitations in the active state. Accordingly, claims 22, 23, and 26-28 are amended to place such method steps in the active tense. Claims 24 and 25 further define structural limitations and therefore do not need to be placed in the active tense. However, claims 24 and 25 are amended to clarify that a structural limitation is being recited, not a method limitation. And claim 29, as written, is already in the active tense.

Applicant believes that such amendments to claims 2, 4, 5, 14, and 22-29 satisfy the requirements of the examiner, and respectfully request that the indefiniteness rejections over those claims be withdrawn.

Response to the Non-Statutory Double Patenting Rejection

Claims 1-14 and 18-34 stand rejected under the judicially created doctrine of double patenting over claims 1-13 of U.S. Patent No. 5,913,813. Accordingly, provided herewith is a timely filed terminal disclaimer in compliance with 37 C.F.R. 1.321(c) to overcome the Examiner's rejection based on a non-statutory double patenting ground, since the patent is commonly owned with this application. Applicant respectfully requests that the Examiner indicate receipt and acceptance of the terminal disclaimer, and withdrawal of the non-statutory double patenting rejection over claims 1-14 and 18-34 of the present application in his next correspondence.

Response to the Anticipation Rejection

Claim 1 stands rejected under 35 U.S.C. § 102(b) as being clearly anticipated by Ishiwara et al., U.S. Patent No. 5,106,360 (hereinafter "Ishiwara"). Claim 1 also stands rejected under 35 U.S.C. § 102(e) as being clearly anticipated by Weinberger, U.S. Patent No. 5,924,973. Based on the amendments and the following remarks, Applicant respectfully requests reconsideration and withdrawal of the rejections under both Ishiwara and Weinberger.

Applicant's invention relates to an interstitial brachytherapy apparatus for providing radiation treatment to proliferative tissue in a living patient. The apparatus includes a catheter body member, an inner spatial volume disposed at a proximal end of the catheter body member, an outer spatial volume defined by an expandable surface element which surrounds the inner spatial volume, and a radiation source disposed in the inner spatial volume. The radiation source

generates a three-dimensional isodose profile that is substantially similar in shape to the expandable surface element.

Turning to the cited prior art, the Ishiwara device comprises a thermotherapeutic apparatus having a catheter body member, an inner lumen surrounded by an outer lumen, and a radiation source contained within the inner lumen. As disclosed in col. 4, lines 19-23, Ishiwara's apparatus is inserted into a body cavity. See, e.g., Figure 4. Hence, the apparatus does not provide *interstitial* radiation treatment, as Applicant's invention requires, but rather intercavital radiation treatment. Such a distinction is significant when considering the isodose profiles generated by the two devices. In the apparatus of Ishiwara, the isodose profiles do not take the shape of the outer lumen. Rather, the radiation source generates absorbed isodoses along the sides of the outer lumen, and not at the ends. This is because Ishiwara is concerned with tumor growth along a cavity, and therefore would not require radiation at the ends of the lumen.

Applicant respectfully reminds the Examiner that in a related parent application, 08/900,021, wherein Ishiwara was also cited, Applicant had argued that:

> In the Ishiwara et al. '360 patent relied upon for anticipation, the outer chamber defined by the radiation transparent wall 12 cannot provide a uniform radiation profile. The outer balloon 12 in the Ishiwara et al. patent functions only to stabilize the device within and hold a thermal mass (liquid) against surrounding tissue so that it can be warmed or cooled by thermal conduction. There is no teaching or suggestion in the patent of how to provide a uniform radial absorbed dose profile of emissions emanating from the liquid radiation source 38. Moreover, given the banana shape of the Ishiwara device, the profile will be much different proximate the distal and proximal ends of the balloon 12 than in its central tissue contacting region. Thus, it cannot be said that applicants' invention, as claimed, is taught by or inherent in the Ishiwara '360 device.

In that instance, Applicant's arguments with respect to Ishiwara were deemed persuasive by the Examiner in the parent application. Applicant believes that much of the arguments

proposed to the Examiner in the parent application are applicable to the present invention. Examiner is asked to kindly refer to Figure 5 of Ishiwara, which shows the banana shape of the device. As illustrated, the outer surface element is not substantially the same shape as the inner spatial volume. Therefore, the radiation source disposed in the inner spatial volume of Ishiwara would not generate a three-dimensional isodose profile that is substantially similar in shape to the expandable surface element.

Similarly, Weinberger discloses in Figure 17 an intercavital radiotherapy device for insertion within a patient's lumen. See col. 4, lines 61-65 and col. 4, lines 22-28. Like Ishiwara, Weinberger's apparatus does not provide *interstitial* radiation treatment, as Applicant's invention requires, but instead *intraluminal* radiation treatment. Whereas Applicant's device treats disease that is embedded in tissue (e.g., breast cancer), Ishiwara and Weinberger treat disease in a luminal cavity. For this reason, in Ishiwara and Weinberger, the catheters and expandable balloons are very different than those of Applicant's invention. Ishiwara and Weinberger require a catheter that can work with a guidewire for insertion into a lumen, while Applicant's catheter does not need to work with a guidewire, since Applicant's apparatus is inserted into tissue rather than a hollow lumen. Effectively, this results in Applicant's catheter being differently sized and shaped relative to the catheters of Ishiwara and Weinberger. Applicant's catheter allows the inner volume to closely match the shape of the outer expandable element, hence allowing the radiation source inside the inner volume to generate a three-dimensional isodose profile that is substantially similar in shape to the outer expandable element.

In contrast, due to the configuration of the catheters, the inner volumes of Ishiwara and Weinberger are not substantially similar in shape to their outer expandable elements. The distinction is significant when considering the three-dimensional isodose profiles generated by the two devices. Ishiwara and Weinberger do not provide an apparatus that can produce isodose

profiles that are substantially similar in shape to the outer lumen. For example, referring to Figure 17 of Weinberger, a large diameter catheter 200 runs through the double balloons 202, 204 of the device. It is clear from this illustration that, given the large size of the Weinberger catheter and the fact that the ends of the balloons do not generate absorbed isodose profiles, the device does not generate a three-dimensional isodose profile that is substantially similar in shape to the outer expandable element.

As amended, independent claims 1 and 21 require an interstitial brachytherapy apparatus having a radiation source disposed in the inner spatial volume that generates a three-dimensional isodose profile that is substantially similar in shape to the expandable surface element. These recitations are neither taught nor suggested by Ishiwara or Weinberger. As discussed *supra*, both Ishiwara and Weinberger disclose an intercavital radiation device that operates differently and generates a different radiative effect than Applicant's interstitial radiotherapy device. Because Ishiwara and Weinberger fail to disclose each and every limitation of the claimed invention, the Examiner is kindly asked to reconsider his rejections under Ishiwara and Weinberger, and withdraw these rejections in his next office action.

Finally, since Ishiwara and Weinberger pertain to intraluminal radiation treatment devices rather than interstitial radiation treatment devices, Applicant urges that Ishiwara and Weinberger fail to disclose or teach an expandable surface element that is adapted to contact tissue surrounding a resected cavity and conform the tissue to the desired shape of the expandable surface element, as is recited in claim 4. In addition, because Ishiwara and Weinberger do not provide an apparatus that can produce isodose profiles that are substantially similar in shape to the expandable surface element, particularly in three dimensions, Applicant urges that claims 5 and 6 are not rendered to be anticipated or obvious by Ishiwara and Weinberger. Therefore, the

Examiner is kindly asked to acknowledge the allowability of these claims in his next office action.

Claim 1 stands rejected under 35 U.S.C. § 102(e) as being clearly anticipated by Bradshaw et al., U.S. Patent No. 5,662,580 (hereinafter "Bradshaw"). Based on the amendments and the following remarks, applicant respectfully requests reconsideration and withdrawal of the rejection under Bradshaw.

As discussed *supra*, Applicant's invention relates to an interstitial brachytherapy apparatus for providing radiation treatment to proliferative tissue in a living patient. The apparatus includes a catheter body member, an inner spatial volume disposed at a proximate end of the catheter body member, an outer spatial volume defined by an expandable surface element which surrounds the inner spatial volume, and a radiation source disposed in the inner spatial volume and generating a three-dimensional isodose profile that is substantially similar in shape to the expandable surface element.

In contrast to Applicant's invention, Bradshaw discloses an intercavital radiotherapy device for insertion within a patient's blood vessel, rather than an interstitial radiotherapy apparatus. See col. 5, lines 11-14. Bradshaw's device thus does not create absorbed isodose profiles shaped substantially similar to the outer lumen of the device. The Examiner is kindly referred to the discussion *supra* for reasons why an intercavital radiotherapy device functions in a different manner than an interstitial radiotherapy device, and hence produces a different isodose profile. Furthermore, Bradshaw discloses in col. 5, lines 15-30 that the *outer* lumen of the balloon catheter is filled with isotopes, rather than the inner lumen, as required in claim 1. Bradshaw therefore teaches the exact opposite of Applicant's claimed invention. Rather than have the isotopes radiate out from an internal lumen, the isotopes in Bradshaw are placed within

the outer lumen contacting the vessel wall. For this reason, Applicant respectfully argues that the claimed invention is neither anticipated by or rendered obvious by Bradshaw. The Examiner is kindly asked to reconsider his rejection under Bradshaw and withdraw this rejection in his next office action.

Finally, since Bradshaw relates to an intraluminal radiation treatment device rather than an interstitial radiation treatment device, Applicant urges that Bradshaw fails to disclose or teach an expandable surface element that is adapted to contact tissue surrounding a resected cavity and conform the tissue to the desired shape of the expandable surface element, as is recited in claim 4. In addition, because Bradshaw does not provide an apparatus that can produce isodose profiles that are substantially similar in shape to the expandable surface element, especially in three dimensions, Applicant urges that claims 5 and 6 are not rendered to be anticipated or obvious by Bradshaw. Therefore, the Examiner is kindly asked to acknowledge the allowability of these claims in his next office action.

Claims 1 and 21-24 stand rejected under 35 U.S.C. § 102(b) as being clearly anticipated by Williams, U.S. Patent No. 5,429,582. Based on the amendments and the following remarks, applicant respectfully requests reconsideration and withdrawal of the rejection under Williams.

Amended claims 1 and 21 now require that the interstitial brachytherapy apparatus comprise a radiation source disposed in the inner spatial volume and generating a three-dimensional isodose profile that is substantially similar in shape to the expandable surface element. As seen in Figure 7 of Williams, outer lumen 28B is not evenly spaced apart from inner lumen 28A that contains the radiation source. In this system, where the radiation source is provided as a liquid within the inner balloon, the shape of the three-dimensional isodose profile will correspond to the shape of the inner balloon. For this reason, Williams does not provide an

11

apparatus that can generate a three-dimensional isodose profile that is substantially similar in shape to the expandable surface element, as is recited in the claims. That is, because the balloons are not equally spaced apart, Williams' apparatus cannot create an isodose profile that has substantially the same shape as the outer element. Hence, Williams fails to disclose each and every limitation of the claimed invention. Based on Applicant's arguments, the Examiner is kindly asked to reconsider his rejection under Williams and withdraw this rejection in his next office action.

Finally, since compression of the brain tissue surrounding the outer balloon 28B (see Figure 7) might prove detrimental to the health of the patient, Applicant urges that Williams fails to disclose or teach an expandable surface element that is adapted to contact tissue surrounding a resected cavity and conform the tissue to the desired shape of the expandable surface element, as is recited in claims 4 and 28. In addition, because William does not provide an apparatus that can produce isodose profiles that are substantially similar in shape to the expandable surface element, particularly in three dimensions, Applicant urges that claims 5, 6, 29, and 30 are not rendered to be anticipated or obvious by Williams. Therefore, the Examiner is kindly asked to acknowledge the allowability of these claims in his next office action.

Response to the Obviousness Rejections

Claim 25 stands rejected under 35 U.S.C. § 103(a) as being unpatentable over Williams. On page 4 of the Office Action, the examiner asserts that:

> Although Williams does not specifically disclose using the device to treat the breast, a modification of Williams to do so would have been obvious to one of ordinary skill in the art at the time the invention was made in that one skilled in the art would readily know that the device could be used in any part of the body to treat tissue surrounding a cavity left by surgical removal of a tumor.

Applicant respectfully disagrees with the examiner's assertions and kindly refers the examiner to the discussion *supra* for reasons why Williams fails to satisfy the limitations of claim 21, as amended. Inasmuch as claim 25 depends upon claim 21, which claim was previously argued by applicant to be unanticipated by Williams, discussion of the rejection of claim 25 over the same prior art is rendered unnecessary. The Examiner is asked to kindly reconsider his rejection of claim 25 over Williams, and withdraw this rejection in his next office action.

Additionally, claims 15-18 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Weinberger or Bradshaw in view of Clerc et al., U.S. Patent No. 6,059,812 (hereinafter "Clerc"). On pages 4 and 5 of the Office Action, the examiner asserts that:

> Bradshaw et al and Weinberger disclose the claimed device except for the use of an expandable cage instead of a balloon. Clerc et al. discloses a self-expanding "cage" (12) that is used to help deliver radioactive therapy. Clerc et al. discloses the support having a shape memory such that it is self opening. Further to use any known shape memory material such as nitinol would have been obvious since nitinol is well known and conventionally used with radioactive therapy devices. Therefore a modification of Bradshaw et al or Weinberger such that a "cage" or support is used instead of a balloon would have been obvious.

For several reasons, applicant respectfully disagrees with the examiner's assertion that these combinations would satisfy the limitations of the claimed invention. In particular, Applicant respectfully disagrees with the examiner's assertions that Bradshaw and Weinberger disclose the claimed device except for the use of an expandable cage instead of a balloon. The Examiner is kindly referred to the discussion *supra* for reasons why both Weinberger and Bradshaw fail to clearly anticipate the claimed invention. Thus, inasmuch as claims 15-18 depend upon claim 1, which claim was previously argued by applicant to be unanticipated by Weinberger and Bradshaw, discussion of the rejection of claims 15-18 over the same prior art is rendered unnecessary.

Because the admitted deficiencies of Weinberger and Bradshaw are not overcome by their combination with Clerc, applicant respectfully requests that the examiner withdraw the obviousness rejections under Weinberger and Bradshaw in view of Clerc in his next office action.

Finally, in reviewing the prior art cited by the examiner, Applicant urges that none of the references either anticipate or render obvious the

Newly Added Claims are Not Anticipated by the Prior Art

Newly added claim 35 depends upon claim 26, which claim was not rejected over prior art, and should therefore be allowable. New claim 36 includes all the limitations of claim 21 and claim 26, which claim was not rejected under prior art. Similarly, newly added claim 38 includes all the limitations of claims 21 and claim 28, which claim was not rejected under prior art. New claim 40 includes all the limitations of claims 1 and 2, which claim was not rejected over prior art. New claims 37 and 39 depend from new claims 36 and 38, respectively. Therefore, Applicant believes that new claims 35-40 are allowable over the cited prior art.

Application No: 09/293,524
Group Art Unit: 3736
Examiner: J. Lacyk
Atty Docket No: 101360-15 (ONE-008)

For all of the foregoing reasons, Applicants request that the Examiner reconsider the rejection of claims 1-34 and allow claims 1-34, along with newly added claims 35-40 to issue. If the Examiner believes that an interview would facilitate the resolution of any outstanding issues, the Examiner is kindly requested to contact the undersigned.

Respectfully submitted,

NUTTER, MCCLENNEN & FISH, LLP

Date: December 20, 2000

Ronald E. Cahill
Reg. No. 38,403
Attorney/Agent for Applicant(s)

One International Place
Boston, MA 02110-2699
Tel: (617) 439-2782
Fax: (617) 310-9782

926429.1

Exhibit 39

US005931774A

United States Patent [19]

Williams et al.

[11] Patent Number: 5,931,774

[45] Date of Patent: Aug. 3, 1999

[54] **INFLATABLE DEVICES FOR TUMOR TREATMENT**

[75] Inventors: **Jeffery A. Williams**, Baltimore, Md.; **Christopher H. Porter**, Woodinville, Wash.; **Mark A. Rydell**, Golden Valley, Minn.

[73] Assignee: **Proxima Therapeutics, Inc.**, Alpharetta, Ga.

[21] Appl. No.: **08/727,259**

[22] Filed: **Oct. 7, 1996**

Related U.S. Application Data

[63] Continuation-in-part of application No. 08/307,165, Sep. 14, 1994, Pat. No. 5,611,767, which is a continuation of application No. 07/715,923, Jun. 14, 1991, Pat. No. 5,429,582.

[51] **Int. Cl.**[6] **A61N 5/02**

[52] **U.S. Cl.** **600/2**

[58] **Field of Search** 600/1–8; 604/19–20; 607/1–3, 88, 96, 99, 100, 103, 105, 107, 113, 114

[56] **References Cited**

U.S. PATENT DOCUMENTS

2,043,630	6/1936	Raiche	18/58
2,677,375	5/1954	Raiche	128/349
3,173,418	3/1965	Baran	128/351
3,324,847	6/1967	Zoumboulis	128/1.2
3,640,269	2/1972	Delgado	128/2
3,831,629	8/1974	Mackal et al.	137/525
3,872,856	3/1975	Clayton	128/1.2
4,022,190	5/1977	Meyer	128/2 A
4,085,757	4/1978	Pevsner	604/96
4,103,689	8/1978	Leighton	128/350 V
4,133,315	1/1979	Berman et al.	604/96
4,206,762	6/1980	Cosman	128/660
4,213,461	7/1980	Pevsner	128/348
4,217,889	8/1980	Radovan et al.	128/1
4,281,667	8/1981	Cosman	128/348
4,292,960	10/1981	Paglione	128/1.1
4,382,445	5/1983	Sommers	604/8
4,417,576	11/1983	Baran	128/207.15
4,541,429	9/1985	Prosl et al.	604/249

(List continued on next page.)

FOREIGN PATENT DOCUMENTS

0 205 384	12/1986	European Pat. Off. .
0 340 881	11/1989	European Pat. Off. .
0 366 814	5/1990	European Pat. Off. .
37 25 691	3/1988	Germany .
2 105 201	3/1983	United Kingdom .

(List continued on next page.)

OTHER PUBLICATIONS

Exhibit A—catalog page of American Heyer–Schulte.

Garfield, et al., "Postoperative intracavitary chemotherapy of malignant glimos", *J. Neurosurg.*, vol. 39, Sep., 1973, pp. 315–322.

NASA Tech Briefs, Jun., 1990, at p. 106.

Shimm et al., "Scanned Focessed Ultrasound Hyperthermia: Initial Crucial Results", *Int. J. Radiation Oncology Bio. Phys.*, Nov. 1988, vol. 15, pp. 1203–1208.

Roberts et al., "Interstitial hyperthermia and iridium brachytherapy in treatment of malignant gliomas" *J. Neorosurg.*, vol. 64, Apr. 1986.

(List continued on next page.)

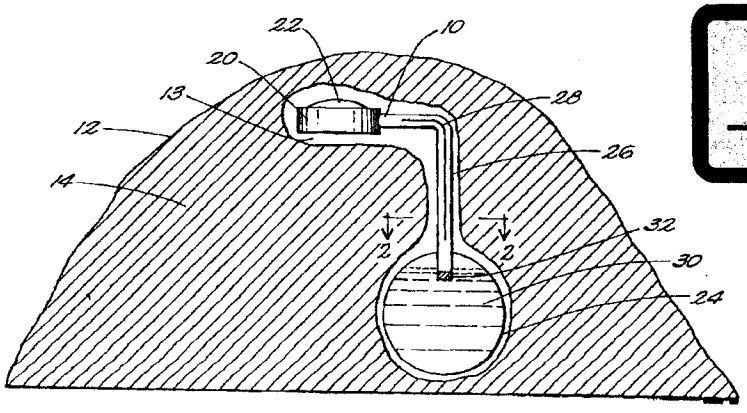
Primary Examiner—John P. Lacyk

Attorney, Agent, or Firm—Thomas J. Engellenner; Nutter, McClennen & Fish,LLP

[57] **ABSTRACT**

Implantable devices for treatment of proliferative disorders are described. In one aspect, the invention provides an implantable apparatus for treating a proliferative disorder in a patient. The device comprises a treatment fluid receptacle for receiving a treatment fluid, an inflatable balloon having a balloon body, a catheter connected between the treatment fluid receptacle and the balloon and defining a fluid flow path therebetween, and a diffusion barrier disposed in the fluid flow path between the treatment fluid receptacle and the balloon. Methods for treating proliferative disorders with the devices are also disclosed.

43 Claims, 2 Drawing Sheets



U.S. PATENT DOCUMENTS

4,558,693	12/1985	Lash et al.	128/79
4,564,022	1/1986	Rosenfeld et al.	128/748
4,588,394	5/1986	Schulte et al.	604/9
4,593,703	6/1986	Cosman	128/748
4,601,713	7/1986	Fuqua	604/280
4,602,655	7/1986	Mackal	137/515
4,617,015	10/1986	Foltz	604/100
4,619,247	10/1986	Inoue et al.	128/6
4,653,508	3/1987	Cosman	128/748
4,655,745	4/1987	Corbett	604/49
4,655,748	4/1987	Mushika	604/96
4,660,568	4/1987	Cosman	128/748
4,681,132	7/1987	Lardner	137/271
4,681,560	7/1987	Schulte et al.	604/9
4,699,615	10/1987	Fischell et al.	604/131
4,706,652	11/1987	Horowitz	128/1.2
4,710,177	12/1987	Smith et al.	604/185
4,754,745	7/1988	Horowitz	128/1.2
4,754,752	7/1988	Ginsburg et al.	128/303.12
4,763,642	8/1988	Horowitz	128/1.2
4,776,369	10/1988	Lardner et al.	137/515.5
4,788,063	11/1988	Fisher et al.	424/449
4,800,899	1/1989	Elliott	600/2
4,816,016	3/1989	Schulte et al.	604/9
4,821,725	4/1989	Azam et al.	128/420
4,846,191	7/1989	Brockway et al.	128/748
4,867,741	9/1989	Portnoy	604/10
5,084,015	1/1992	Moriuchi	604/96
5,106,360	4/1992	Ishiwara et al.	600/2
5,112,303	5/1992	Pudenz et al.	604/49
5,125,888	6/1992	Howard et al.	600/12
5,152,747	10/1992	Olivier	604/93
5,236,410	8/1993	Granov et al.	600/12
5,429,582	7/1995	Williams	600/2

FOREIGN PATENT DOCUMENTS

WO 90 04365	5/1990	WIPO .
WO 91 05528	5/1991	WIPO .
WO 92 10932	7/1992	WIPO .
92/22350	12/1992	WIPO .
WO 93 09724	5/1993	WIPO .

OTHER PUBLICATIONS

Chun et al., "Interstitial iridum–192 implantation for malignant brain tumours Part II", *The British Journal of Radiology*, Feb., 1989, pp. 158–162.

Am. J. Clin. Oncol., (CCT), vol. 10, No. 2, 1987, at p. 106, item (13).

Gutin et al. "Brachytherapy of recurrent malignant brain tumors with removable high–activity iodine–125 sources", *J. Neurosurg*, vol. 60, pp. 61–68, Jan. 1984.

Wu et al., "Interstitial iridium–192 implantation for malignant brain tumours Part I", *The British Journal of Radiology*, pp. 154–157, Feb. 1989.

Raaphorst et al. "A Comparison of Heat and Radiation Sensitivity of Three Human Glioma Cell Lines", *J. Radiation Oncology Biol. Phys.*, vol. 17, pp. 615–622.

Moidel et al., "Materials for Selective Tissue Heating in a Radiofrequency Electromagnetic Field for the Combined Chemothermal Treatment of Brain Tumors", *J. Biomed Mater. Res.*, vol. 10, pp. 327–334, 1976.

Exhibit B—Brochure of Halkey–Roberts Corporation of St. Petersburg, Florida.

European Search Report Application No. EP 92 91 3085 dated Dec. 12, 1995.

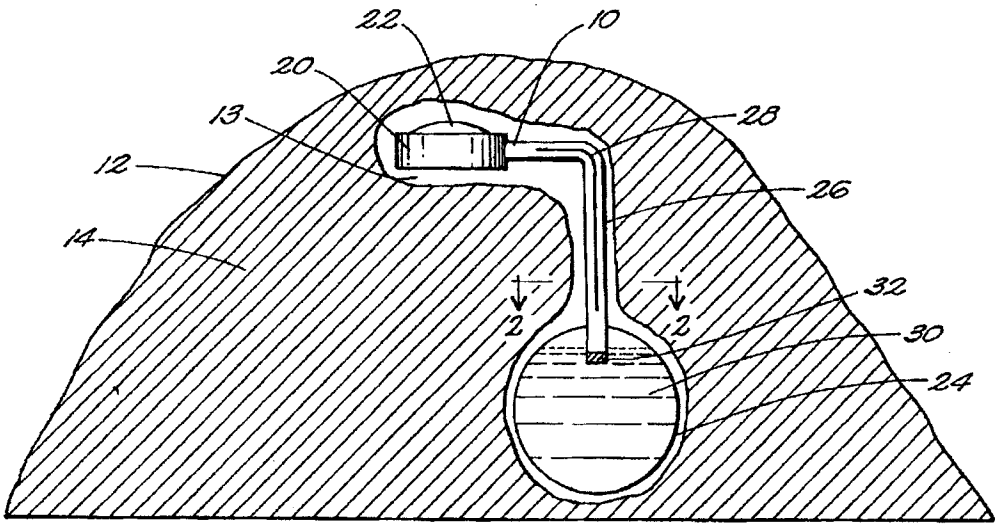


FIG. 1

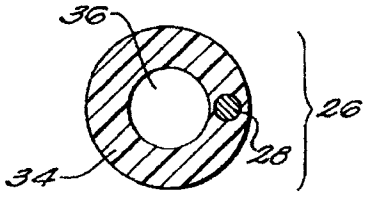


FIG. 2A

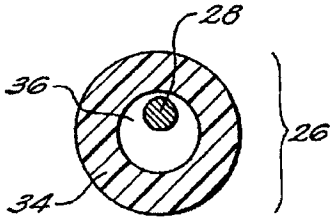


FIG. 2B

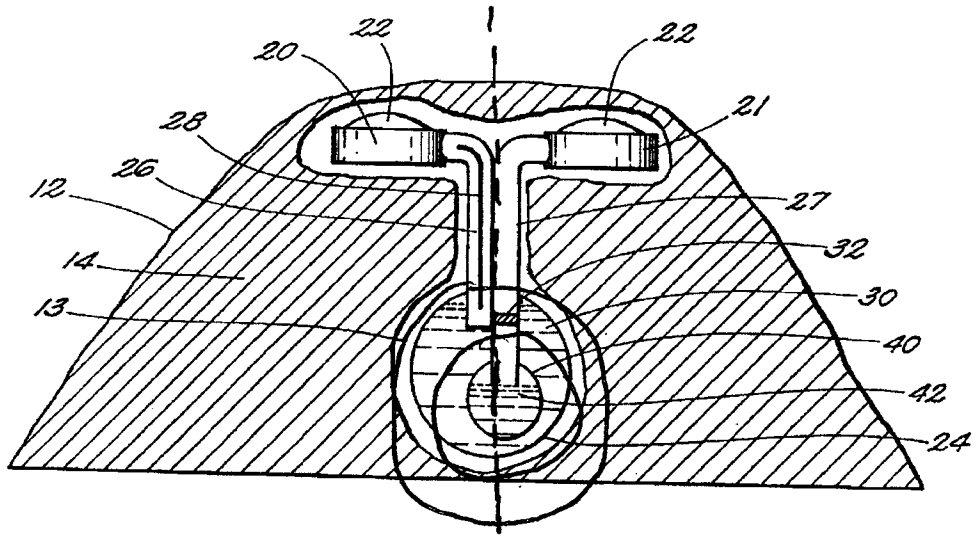


FIG. 3

INFLATABLE DEVICES FOR TUMOR TREATMENT

RELATED APPLICATIONS

This application is a continuation-in-part of U.S. Ser. No. 08/307,165, filed Sep. 14, 1994, now U.S. Pat. No. 5,611,767, which is a continuation of U.S. Ser. No. 07/715,923, filed Jun. 14, 1991, now U.S. Pat. No. 5,429,582, the contents of which are hereby incorporated by reference.

BACKGROUND OF THE INVENTION

Treatment of proliferative disorders has become increasingly sophisticated in recent years, and improvements in surgical, chemotherapeutic and brachytherapeutic techniques have led to better outcomes in patients suffering from such disorders. The need for improved devices for administration of chemotherapy and brachytherapy has resulted in a number of new devices capable of delivering one or more treatments to proliferative disease sites, such as tumors. One such device is described in U.S. Pat. No. 5,429,582 to Williams, which discloses an inflatable device for multimodal therapy of tumors. Nevertheless, improved devices for treatment of proliferative disorders are needed.

SUMMARY

This invention provides improved devices for the treatment of tumors and other proliferative disorders in a patient in need of such treatment, and methods of treating proliferative disorders using such devices.

In one aspect, the invention provides an implantable apparatus for treating a proliferative disorder in a patient. The device comprises a treatment fluid receptacle for receiving a treatment fluid, an inflatable balloon having a balloon body, a catheter connected between the treatment fluid receptacle and the balloon and defining a fluid flow path therebetween, and a diffusion barrier disposed in the fluid flow path between the treatment fluid receptacle and the balloon.

In certain embodiments, the treatment fluid receptacle has a small volume and is adapted to be implanted subcutaneously in the body of the patient. In certain embodiments, the device further includes a malleable element. In certain embodiments, the diffusion barrier is a narrow flow segment. In certain embodiments, the balloon has a substantially spherical shape when inflated. In other embodiments, the balloon has a substantially ovoid shape when inflated. In some embodiments, the balloon is secured to the catheter at substantially a single point on the balloon body. In other embodiments, the balloon is secured to the catheter at a plurality of points on the balloon body. In certain embodiments, the balloon has an irregular shape when inflated.

The balloon body can be substantially impermeable to the treatment fluid, while in other embodiments, the balloon can comprise a semipermeable membrane. In certain embodiments, the treatment fluid receptacle can be flushed with a flushing fluid without substantially expanding the balloon. In some embodiments, the balloon is secured to the catheter such that the balloon maintains a pre-selected shape during inflation. In preferred embodiments, the malleable element, if present, does not interfere with NMR measurements.

In certain embodiments, the balloon comprises a double-walled balloon or a triple-walled balloon. In some embodiments, the proliferative disorder is a brain tumor. In

certain embodiments, the balloon is adapted for placement in a cavity left by surgical removal of a tumor from the patient. In other embodiments, the balloon is adapted for placement in a natural body cavity. In preferred embodiments, the balloon is filled with a treatment fluid. In certain embodiments, the treatment fluid is a radioactive fluid. In some embodiments, the treatment fluid has substantially physiological tonicity.

In certain embodiments, the apparatus further comprises a second treatment fluid receptacle. In certain embodiments, the second treatment fluid receptacle fluidly communicates with a volume between inner and outer balloon walls.

In another embodiment, the invention provides an implantable apparatus for treating a proliferative disorder in a patient. The implantable apparatus includes a treatment fluid receptacle for receiving a treatment fluid, an inflatable balloon having a balloon body; a catheter connected between the treatment fluid receptacle and the balloon and defining a fluid flow path therebetween; and a diffusion barrier disposed in the fluid flow path between the treatment fluid receptacle and the balloon, and in which the balloon is secured to the catheter such that the balloon maintains a pre-selected shape during inflation; and in which the treatment fluid receptacle is adapted to be flushed with a small volume of a flush fluid.

In another aspect, the invention provides a method for treating a proliferative disorder, such as a tumor, in a patient. The method includes the steps of implanting in the patient's body an inflatable treatment apparatus, in which the apparatus includes a treatment fluid receptacle for receiving a treatment fluid; an inflatable balloon having a balloon body; a catheter connected between the treatment fluid receptacle and the balloon and defining a fluid flow path therebetween; and a diffusion barrier disposed in the fluid flow path between the treatment fluid receptacle and the balloon; and introducing a treatment fluid into the treatment fluid receptacle such that the balloon is inflated; such that the proliferative disorder is treated.

In certain embodiments, the method includes the further step of flushing the treatment fluid into the balloon.

In another aspect, the invention provides a method for treating a proliferative disorder in a patient. The method comprises determining a characteristic of a cavity in the patient's body, the characteristic being selected from the group consisting of volume, shape, or a dimension; selecting an inflatable balloon suitable for placement in the cavity, the balloon including a balloon body. The method includes the further steps of implanting in the cavity an inflatable treatment apparatus comprising a treatment fluid receptacle for receiving a treatment fluid; the inflatable balloon; a catheter connected between the treatment fluid receptacle and the balloon and defining a fluid flow path therebetween; and a diffusion barrier disposed in the fluid flow path between the treatment fluid receptacle and the balloon. The method further includes the step of introducing a treatment fluid into the treatment fluid receptacle such that the balloon is inflated, such that the proliferative disorder is treated.

In certain embodiments, the method includes, prior to the implanting step, the further step of assembling the inflatable treatment apparatus.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. **1** is a schematic cross-sectional view of one embodiment of the treatment devices of the invention.

FIGS. **2A** and **2B** show cross-sectional views along the line **2—2'** of embodiments of the catheter of the invention.

FIG. 3 is a schematic cross-sectional view of a double-balloon embodiment of a treatment device of the invention.

DETAILED DESCRIPTION OF THE INVENTION

The ability to selectively deliver therapy to a target organ or site, e.g., a tumor, is of great value to physicians. Accordingly, the invention provides methods and apparatuses suitable for delivery of one or more therapeutic modalities in a selective fashion.

For convenience, certain terms employed in the specification, examples, and appended claims are collected here.

The term "proliferative disorder" is recognized in the art, and, as used herein, refers to a disorder including or characterized by rapid or abnormal cell growth or proliferation. Exemplary proliferative disorders include, but are not limited to, tumors, e.g., cancerous tumors; restenosis, e.g., regrowth of smooth muscle cells of blood vessels after angioplasty; abnormal angiogenesis; hyperplasia, e.g., benign prostatic hyperplasia; and the like.

The term "treatment fluid," as used herein, refers to a fluid used for therapy of a proliferative disorder. Treatment fluids include chemotherapy fluids such as are conventional in the art, as well as fluids suitable for radiation therapy (brachytherapy), e.g., fluids comprising a radioisotope useful in treatment of proliferative disorders.

The term "treatment fluid receptacle," as used herein, refers to a receptacle or chamber adapted for receiving a treatment fluid. Treatment fluid receptacles are known in the art, and include injection ports and similar devices. A "small-volume" treatment fluid receptacle has a volume or hold-up less than conventional treatment fluid receptacles, e.g., less than about 5 ml, more preferably less than about 2 ml, and still more preferably less than 1.5 ml. Thus, treatment fluid receptacles having little dead space or low hold-up volumes are generally preferred for use in the methods and devices of the invention. Particularly preferred treatment fluid receptacles can be flushed with a small volume of flush fluid, as described in more detail below.

The term "diffusion barrier," as used herein, refers to an element adapted for decreasing or preventing diffusion or flow of fluid from a balloon into the catheter lumen or treatment fluid receptacle of the subject inflatable treatment device.

A balloon that maintains a "substantially constant shape," as used herein, refers to a balloon that maintains substantially a single shape or profile over a range of inflation sizes. Thus, for example, a balloon that maintains a substantially spherical shape upon inflation has a generally spherical shape over a range of inflation sizes, from low inflation to full inflation, and does not generally change shape as inflation is increased or decreased. It will be understood by the skilled artisan, however, that the initial shape of a balloon can be chosen to minimize the size or profile of the deflated balloon, e.g., to ease insertion of the balloon into a body cavity. Thus, a balloon can have an initial shape different from a "substantially constant shape," and still assume a "constant shape" after partial inflation. A "predetermined shape" refers to a shape that can be selected by the practitioner before balloon insertion, e.g., a shape chosen to ensure compliance of the balloon body to a selected surface, e.g., a cavity surface.

The term "narrow flow segment", as used herein, refers to a narrowed or restricted portion of a flow path. Preferably, a narrow flow segment has a flow passage sufficiently small to slow or prevent significant flow or diffusion of a fluid through the passage without application of pressure.

The term "malleable element," as used herein, refers to an element, e.g., a wire, that is malleable or flexible, i.e., capable of being shaped by bending, flexing, pressing and the like, and maintaining, temporarily or permanently, the shape thus provided. In preferred embodiments, a malleable element can be shaped by hand, e.g., by a surgeon performing a surgical procedure, to impart a selected shape to the malleable element and to the catheter of which it forms a part.

The term "flushing fluid," as used herein, refers to fluid that can be used to flush, rinse, or wash a flow portion of an inflatable treatment device. A flushing fluid can be inert, e.g., a saline solution, or can itself be a treatment fluid. In general, an inert flushing fluid is preferred.

The term "patient," as used herein, refers to an animal in need of treatment for, or susceptible to, a proliferative disorder. In preferred embodiments, the patient is a warm-blooded animal, more preferably a mammal, including humans and non-human mammals such as dogs, cats, pigs, cows, sheep, goats, rats, and mice. In a particularly preferred embodiment, the subject is a human.

The inflatable treatment devices of the invention provide certain advantages over devices known in the art. The subject devices are adaptable to a wide variety of therapeutic treatments, and are simple and safe to use. In general, the devices are implanted in a patient's body such that the balloon is in close proximity to the site to be treated, e.g., the tumor, blood vessel, and the like. In one embodiment, the balloon is placed in a natural body cavity or a cavity resulting from surgical removal or displacement of tissue, e.g., surgical debulking of at least a portion of a tumor, or angioplasty to displace or compress a growth of a blood vessel.

Thus, for example, FIG. **1** shows a cross-sectional view of an inflatable device of the invention when implanted in a body cavity. In this embodiment, the device **10** is implanted below the skin **12** in a cavity **13** formed in the patient's tissue **14**. The device **10** includes an injection port **20** which has an elastomeric seal **22** secured thereto. A balloon **24** is disposed in the cavity **13** and fluidly connected to the injection port **20** through a catheter **26**, which includes a malleable element **28**. The balloon is filled with a treatment fluid **30**, which fluid is prevented from flowing back from the balloon **24** into the catheter **26** by a diffusion barrier **32**.

In certain embodiments, a treatment fluid receptacle is implanted subcutaneously, permitting ready injection of a treatment fluid while allowing healing of a surgical incision. Treatment fluid receptacles suitable for use in the devices of the invention are known in the art. For example, injection ports, which can be subcutaneously implanted, have been described in, e.g., U.S. Pat. Nos. 4,816,016 and 4,681,560 to Schulte, and are commercially available (e.g., from C. R. Bard Co.). An injection port for implantation in vivo should be constructed of materials that will not provoke an immune response or tissue reaction. An injection port preferably has an elastomeric seal secured to a base and defining an injection chamber of predetermined volume. The elastomeric seal can be adapted to sealingly engage a needle that pierces the seal, e.g., a hypodermic needle, and to reseal when the needle is removed, thereby preventing leakage. In general, preferred treatment fluid receptacles can be readily and efficiently flushed with a small volume of flush fluid, e.g., can be flushed with less than about 5 ml of flush fluid, more preferably less than about 2 ml, and still more pref-

erably less than 1.5 ml. The amount of flush fluid required will be determined, at least in part, by such factors as the total volume of the treatment fluid receptacle, the amount of "dead space" in the treatment fluid receptacle, the nature of the treatment fluid and the flush fluid, and the like. In preferred embodiments, the volume of the treatment fluid receptacle, e.g., the injection chamber, is minimized, e.g., has a small volume. By providing a small-volume treatment fluid receptacle, the volume of treatment and flushing fluids is minimized, preventing overinflation of the balloon and decreasing the volume of fluids that must be handled by the physician. Preferred treatment fluid receptacles have a volume of at least 0.5 ml, but not more than 5 ml, more preferably between about 1 and about 3 ml. In general, it is desirable for the injection port to be palpable through the skin, so that it can be easily located. The treatment fluid receptacle can be at least partially opaque to X-rays, permitting localization by radiography.

As mentioned above, in certain embodiments it is desirable, after treatment fluid has been injected into the treatment device, to flush the injection port to displace a treatment fluid from the injection port and catheter. For example, when the treatment fluid is a radioactive fluid, it is desirable to prevent radiation damage to healthy tissue adjacent to the treatment fluid receptacle and along the catheter path. To prevent damage to healthy tissue, the treatment fluid can be flushed out of the injection port and away from such tissue. The flush fluid can be flushed through the catheter and into the balloon, thereby flushing the catheter and increasing the amount of radioactive material in the balloon. A small-volume treatment fluid receptacle can be flushed rapidly and completely using small volumes of flush solution, thereby reducing the amount of additional fluid added to the balloon. Thus, a small-volume treatment fluid receptacle is preferred for use with radioactive treatment fluids. Alternatively, the flush fluid can be removed from the treatment device, e.g., by use of a needle, positioned in the injection port, for withdrawing excess fluid. In this embodiment, two needles can be employed simultaneously: one needle for injection of a flush fluid into the injection port, and a second needle for removal of the fluid. In this embodiment, further inflation of the balloon can be prevented.

The inventive devices can include a diffusion barrier, to prevent unwanted backflow of treatment fluid from the balloon into the catheter. The diffusion barrier thereby prevents premature deflation of the balloon and isolates the treatment fluid in the balloon. In particular, the diffusion barrier can reduce or prevent diffusion or flow of a treatment fluid, especially a radioactive treatment fluid, from the balloon into the catheter or other parts of the implantable device, thereby preventing damage to healthy tissue adjacent to the catheter track. The diffusion barrier can be any element or elements adapted to retard or prevent fluid flow, including, without limitation, a valve (e.g., a check valve) or other flow regulating element, a narrow flow segment, and the like. A valve can be manually or automatically operated to permit control of fluid flow, if desired, e.g., during balloon filling, flushing of an injection port, or removal of fluid from the device. In certain embodiments, the diffusion barrier is an elastomeric material disposed in the fluid flow path and having a slit, e.g., a slit of proportions similar to a Holter valve opening. In this embodiment, fluid flow through the diffusion barrier can be accomplished by the application of fluid under pressure, e.g., by providing a fluid under pressure with a hypodermic syringe, causing the elastomer to yield sufficiently to permit fluid flow. Preferably, the pressure required to cause fluid flow through the diffusion barrier is not so high as to present risk of rupture of the therapeutic device, but is sufficient to reduce unwanted flow from the balloon. The diffusion barrier can provide resistance to fluid flow in one direction (e.g., a one-way check valve) or in both directions. However, the diffusion barrier is preferably adapted to allow removal of fluid from the balloon when the therapeutic procedure is complete, preferably without requiring removal of the balloon from the body cavity. Thus, in certain embodiments, the diffusion barrier is not a check valve. The diffusion barrier can reduce or eliminate flow from the balloon for at least a short period of time, e.g., sufficient time for therapeutic treatment to be completed.

In certain embodiments, the inventive apparatus can include a malleable element extending through at least a portion of the length of the catheter lumen. Thus, the malleable element is preferably adapted to confer a shape upon at least a portion of the catheter length. The malleable element is preferably an integral component of the catheter, and is not a stylet or guidewire. The malleable element can provide increased stiffness to the catheter, thereby preventing kinking of the catheter and concomitant blockage of the lumen, during insertion or removal. In particular, the malleable element can eliminate the need for a separate guidewire or stylet for inserting the catheter, simplifying surgical procedures. However, the malleable element should not be excessively rigid, to avoid damaging fragile tissues. The malleable element further can permit a shape to be temporarily or permanently imparted to the catheter. Thus, the catheter can be easily and accurately placed in the patient's body. For example, the malleable element can be conformed to a shape of a body lumen, or can be formed to permit the balloon to be placed at a body site not readily accessible by conventional means. Also, the malleable element can provide a means for securing or anchoring the implantable device in a patient's body and preventing the catheter from "backing out" during or after surgical placement.

The malleable element can comprise, a flexible wire, which can be embedded in a wall of the catheter, secured to an inner or outer surface of a sidewall of the catheter, or can be situated in the lumen of the catheter. Thus, for example, FIG. **2A** depicts a cross-sectional view of one embodiment of a catheter along line **2**—**2** of FIG. **1**. The sidewall **34** of the catheter **26** defines a catheter lumen **36**. A malleable wire **28** is embedded in the sidewall **34**. FIG. **2B** depicts a catheter in which a malleable element **28** is secured to the sidewall **34** in the catheter lumen **36** of catheter **26**. The wire can be made of, stainless steel, titanium and other metals, and alloys thereof. A preferred malleable element is a titanium wire, e.g., a 20 mil annealed titanium wire. In one embodiment, the malleable element comprises a metallic element or alloy, such as nitinol, which exhibits "shape memory," i.e., has the property of returning to a predefined shape upon heating. In this embodiment, the wire can be selected to have a desired shape when implanted, but can be bent to a different shape prior to insertion to accommodate placement in vivo, and then heated (e.g., with a resistive heater) to restore the preselected shape. In certain preferred embodiments, the malleable element comprises a metallic element or alloy which does not substantially interfere with NMR measurements, e.g., magnetic resonance imaging; i.e., NMR measurements of the patient's body can be performed while the malleable element is present in the patient's body. In this embodiment, non-ferromagnetic metals or alloys are preferred. A preferred malleable element comprises an annealed titanium wire, preferably about 20 mil in diameter.

Such a wire can also be employed to provide a source of electric current, e.g., to a resistive heater, or to provide means for monitoring conditions, e.g., temperature, inside the patient's body. Thus, a malleable wire can provide means for additional treatment modalities, e.g., heat therapy, which can be employed in conjunction with chemotherapy and brachytherapy, if desired. Additionally, the malleable element can be employed as a radio-opaque marker for locating the catheter in the body.

The inflatable treatment devices include an inflatable balloon for containing a treatment fluid in close proximity to the tissue to be treated. It will be understood that the term "balloon" is intended to include distensible devices which can be, but need not be, constructed of an elastic material. A variety of balloons or other distensible devices for use with surgical catheters are known in the art and are contemplated for use in the invention; many balloons are commercially available. In one embodiment, the balloon is constructed of a material that is substantially impermeable to the active components of the treatment fluid with which it is filled, and is also impermeable to body fluids, e.g., blood, cerebrospinal fluid, and the like. An impermeable balloon is useful in conjunction with a radioactive treatment fluid, to prevent the radioactive material from escaping the treatment device and contaminating the surgical field or tissues of the patient. In another embodiment, the balloon is permeable to the treatment fluid, and permits the fluid to pass out of the treatment device and into a body lumen or cavity. A permeable balloon is useful when the treatment fluid is a chemotherapeutic agent which must contact tissue to be effective. Semi-permeable balloons can also find use in the inventive devices. For example, a semipermeable material that is capable of preventing the passage of a radioactive material through the balloon wall can be used to contain a radioactive treatment fluid, where certain fluid components can pass through the membrane while the radioactive component is retained within the balloon. In some embodiments, isotonic fluids are preferred for use in semipermeable balloons, as discussed below. Silicone, e.g., NuSil, is a preferred material for a balloon wall.

In general, it is preferable that the balloon have a shape that permits the balloon to conform to the body cavity or lumen in which the balloon is to be inflated. For example, a generally spherical cavity can be filled with a substantially spherical balloon, while an elongated balloon shape is suitable for an elongated body lumen such as a blood vessel. Irregular balloon shapes may also find application in the subject devices and methods. In certain embodiments, a balloon will be selected such that, upon inflation, the balloon does not compress the tissue which is being treated, or surrounding tissues. Thus, when a radioactive treatment fluid is introduced into the device, e.g., by injection, the inflatable treatment device is inflated to a volume not substantially greater than a volume of the body cavity in which the device has been placed, thereby avoiding any substantial compression or distortion of normal tissue. For example, in one embodiment, when the balloon is placed within a cavity left by surgical removal of tissue, the balloon is not inflated to a size substantially larger than the size of the cavity. However, in certain embodiments, the balloon preferably is inflated to compress tissue. For example, when the proliferative disorder being treated is, e.g., restenosis of a blood vessel, the balloon can be inflated to a size large enough to compress the excess tissue, while also providing chemotherapy, brachytherapy, or the like to treat the lesion. Thus, a balloon can be selected to have a desired size, and the amount of treatment fluid can be adjusted to attain an inflation of the balloon to achieve the desired size. In general, the balloon should have a small profile, e.g., a small size, when deflated, to permit facile placement in the patient's body and to minimize the size of a surgical incision needed to place the balloon at the desired site of action.

In some embodiments, a balloon is attached to the catheter at substantially a single point on, or a single side of, the balloon body. Catheters suitable for use in the invention are well known in the art. A preferred catheter material is radio-opaque silicone. Attachment of a balloon to a catheter at a single point on the balloon body permits the balloon (e.g., a spherical balloon) to maintain a substantially constant (e.g., spherical) shape over a range of inflation volumes. That is, the balloon is not constrained in shape by multiple attachment points to the catheter, as is commonly the case with, e.g., balloons for Foley catheters. In other embodiments, the balloon is attached to the catheter at multiple points on the balloon body, while allowing the balloon to maintain a constant shape over a range of inflation sizes. For example, a balloon attached to a catheter at both distal and proximal points on the balloon body can be unconstrained upon inflation where the catheter includes an expansion element (e.g., a slidable engagement element) that permits the catheter to adjust in length as the balloon expands or contracts. A balloon which maintains a substantially constant shape over a range of inflation volumes permits a surgeon to select a balloon to conform to a cavity of a particular shape with less concern over the size of the cavity. Thus, devices that include such a balloon reduce the need for the surgeon to prepare several different-sized balloons prior to surgery.

The invention also contemplates the use of multiple balloons, e.g., a double-walled balloon. Such a balloon can comprise, for example, an impermeable inner wall and a permeable outer wall. In this embodiment, the inner balloon can be filled with, e.g., a radioactive treatment fluid, while the outer balloon (i.e., the space between the inner and outer balloon walls) is filled with a chemotherapeutic treatment fluid. This embodiment allows two modes of therapy (e.g., chemotherapy and brachytherapy) to be administered simultaneously with a single device. In this double-walled balloon embodiment, the device preferably includes two treatment fluid receptacles, one in communication with each of the two balloons, preferably through a separate catheter, one catheter fluidly connected to each balloon and treatment fluid receptacle. The two balloons can thus be inflated with two treatment fluids at the same time or at different times during therapy. Inflation of an inner balloon can provide pressure on an outer balloon, which can cause the outer balloon to expand, or can force or urge fluid in the space between the inner and outer balloon walls through the membrane of a porous outer balloon. Higher-order balloons, e.g., triple-walled balloons, can also be used in the inventive devices.

Thus, for example, FIG. **3** shows a double-balloon device of the invention. The device has two treatment fluid receptacles **20**, **21**, each having an elastomeric seal **22** secured thereto. Receptacle **20** is fluidly connected to outer balloon **24** through catheter **26**, which includes a malleable element **28**, and receptacle **21** is fluidly connected to inner balloon **40** by catheter **27**, which includes diffusion barrier **32**. The device of FIG. **3** is useful where a chemotherapeutic fluid **30** is used to inflate the outer balloon **24**, while a radioactive fluid **42** fills the inner balloon **40**. Diffusion barrier **32** prevents flow of the radioactive fluid **42** from the balloon **40** to the catheter **27**.

The catheter element can be any of a variety of catheters known in the art. A preferred catheter material is silicone,

preferably a silicone that is at least partially radio-opaque, thus facilitating x-ray location of the catheter after implantation of the device. The catheter can also include conventional adapters for attachment to the treatment fluid receptacle and the balloon, as well as devices, e.g., right-angle devices, for conforming the catheter to contours of the patient's body.

In some embodiments, the inventive devices are provided in pre-assembled form, i.e., the components are assembled in advance of a surgical insertion procedure. In certain embodiments, however, the inventive devices are configured to permit modular assembly of components, e.g., by a surgeon. Thus, for example, a treatment fluid receptacle can be provided with an element adapted for connection to any one of a plurality of catheters. The connection element can be, e.g., any element known in the art for effecting connection between components such as catheters, injection ports, and the like. Illustrative connectors include luer adapters and the like. In this embodiment, a variety of catheters and balloons can be provided, each of which is adapted for facile connection to the treatment fluid receptacle. The surgeon can then select an appropriate size and shape of balloon for treatment of a particular proliferative disorder without need for providing several treatment fluid receptacles. The catheter and balloon can be selected according to the results of pre-operative tests (e.g., x-ray, MRI, and the like), or the selection can be made based on observation, during a surgical procedure, of the target cavity (e.g., a surgical cavity resulting from tumor excision). When the surgeon selects an appropriate balloon (e.g., a balloon having a size and shape suitable for placement in a body cavity), the catheter and balloon can then be attached to the pre-selected treatment fluid receptacle, thereby assembling the treatment device.

The above-described implantable inflatable treatment devices can be employed in the treatment of proliferative disorders in a patient. In one aspect, the invention provides a method of treating proliferative disorders including the step of implanting in the patient's body an inflatable treatment apparatus, in which the apparatus includes a small-volume treatment fluid receptacle for receiving a treatment fluid; an inflatable balloon having a balloon body; a catheter connected between the treatment fluid receptacle and the balloon and defining a fluid flow path therebetween; and a diffusion barrier disposed in the fluid flow path between the treatment fluid receptacle and the balloon; wherein the balloon is secured to the catheter such that the balloon maintains a substantially constant shape during inflation; and introducing a treatment fluid into the treatment fluid receptacle so that the balloon is inflated, such that the proliferative disorder is treated. In certain embodiments, the method includes the step of selecting a balloon for treatment a proliferative disorder in a patient. In some embodiments, the method includes, prior to the implanting step, the further step of assembling an inflatable treatment apparatus.

The treatment devices of the invention (or any part thereof, e.g., the balloon) can be implanted according to surgical methods well known to the skilled artisan. In one embodiment, the balloon is implanted in a cavity formed by removal of tissue from a tumor or organ. Thus, in certain embodiments, the method includes the step of surgically removing tissue to form a cavity in the patient's body prior to implanting the inflatable device. In other embodiments, the device is implanted in a natural body cavity, e.g., in the abdominal cavity, or an organ such as a lung, uterus, or prostate gland. In yet other embodiments, a cavity or space, for placement of the inventive device in a patient's body, can be formed by displacing, compressing, or otherwise repositioning tissue, without surgically removing tissue. Illustratively, tissue can be compressed, e.g., by inflation of a balloon, prior to placement of a device of the invention in the cavity formed thereby. In certain embodiments, the treatment fluid receptacle is implanted subcutaneously. It will be appreciated that the catheter or catheters of the device can be implanted so as to pass through a body wall, e.g., the skull, the abdominal wall, and the like.

The treatment fluid (or fluids) for inflating the balloon (or balloons) can be provided to the treatment fluid receptacle by, e.g., transcutaneous injection into an injection port(s). Injection can be with a syringe, e.g., a hypodermic syringe, or with a pump or other mechanical delivery means.

In certain preferred embodiments, the proliferative disorder is a tumor, more preferably a solid tumor, including both benign and malignant tumors. In some embodiments, the tumor is a cancerous tumor. Methods of the invention are useful in treating cancers such as, without limitation, brain tumors, breast tumors, prostate tumors, ovarian tumors, and the like. In another preferred embodiment, the proliferative disorder is restenosis, e.g., of a blood vessel. Thus, the subject method can be employed to treat or to prevent restenosis in a patient. Similarly, the subject method can be employed to treat hyperplasia, including endometriosis, benign prostatic hyperplasia, and the like.

In certain embodiments, the treatment fluid includes a chemotherapy agent. Formulation and dosage of chemotherapy agents is routine to the skilled artisan. In certain embodiments, the treatment fluid includes a radioisotope. Radioactive treatment fluids are useful for brachytherapy, as discussed supra. Preferred radioisotopes for brachytherapy include ^{90}Y, ^{198}Au, ^{32}P, ^{125}I, and ^{131}I. Radioisotope preparations suitable for use in the subject treatment devices are known to those of skill in the art. It will be appreciated that a treatment fluid can be formulated to provide more than one treatment modality. For example, a chemotherapy fluid can be heated to provide both chemotherapy and heat therapy. In certain embodiments, the treatment fluid is approximately isotonic with body fluids; that is, the tonicity (ionic strength) of the treatment fluid is close to that of physiological fluids. Use of isotonic treatment fluids avoids transfer of solutions across the balloon body membrane, thereby preventing unexpected or undesired inflation or deflation of the balloon, or dilution or concentration of the treatment fluid.

In certain embodiments, the method of treatment includes the further step of flushing the treatment fluid receptacle (e.g., the injection port) with a flush fluid. As previously described, it is important to avoid damaging healthy tissue by exposure to high doses of radiation from the treatment fluid. Thus, to prevent damage to tissue adjacent the injection port and the catheter, the injection port and catheter can be flushed with a non-radioactive flush fluid. In certain embodiments, the flush fluid is flushed into the balloon. In this embodiment, the volume of flush fluid should be carefully regulated to ensure that the balloon does not become overinflated. In certain embodiments, the flush fluid inflates the balloon by no more than 20%, more preferably no more than 10%. Alternatively, the flush fluid can be withdrawn from the treatment device, e.g., by removal with a needle introduced into the injection port. In this embodiment, the balloon is preferably not significantly further inflated, e.g., inflation due to the flush solution is less than 10%, more preferably less than 5%, of the volume of the inflated balloon. In some preferred embodiments, e.g., where a radioactive treatment fluid has been employed, the flushing step can reduce the level of radioactivity present in the

treatment fluid receptacle or the catheter by at least about 50%, more preferably by at least 80%, and still more preferably by at least 90%.

In certain embodiments, the flush solution has approximately physiological tonicity. In some embodiments, the flush solution is more viscous than the treatment fluid such that the flow of the flush fluid approaches plug flow. A viscous flush solution can also prevent backflow or diffusion of a radioactive treatment fluid because the higher viscosity impedes flow in the catheter lumen.

The treatment is preferably continued until the proliferative disorder has been significantly ameliorated, e.g., if the proliferative disorder is a tumor, treatment is continued until the tumor has decreased in size by at least about 10%, more preferably at least about 20%. The inflatable device can be left in place and repeated filled with treatment fluid, if desired. For example, repeated doses of a chemotherapy fluid can be administered without disturbing the placement of the device, simply by injecting more treatment fluid into a permeable balloon after-the original dose has passed through he balloon. Similarly, a radioactive fluid can be removed, e.g., to prevent excessive doses of radiation or when the radioisotope has decayed, and replenished by addition of fresh radioisotope solution. Where it is desired to use repeated doses, the strength of the doses can be varied, for example, a first, strong dose, followed by a second, less potent dose. Determination of appropriate dosages strengths and treatment regimens will be routine for the skilled artisan.

The contents of each patent, patent application, and publication cited herein are hereby incorporated by reference.

Those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, numerous equivalents to the methods and devices described herein. Such equivalents are considered to be within the scope of this invention and are covered by the following claims.

What is claimed is:

1. An implantable apparatus for treating a proliferative disorder in a patient, comprising:

a treatment fluid receptacle for receiving a treatment fluid;

an inflatable balloon having a balloon body;

a catheter connected between the treatment fluid receptacle and the balloon and defining a fluid flow path therebetween; and

a diffusion barrier disposed in the fluid flow path between the treatment fluid receptacle and the balloon.

2. The apparatus of claim **1**, wherein the treatment fluid receptacle has a small volume and is adapted to be implanted subcutaneously in the body of the patient.

3. The apparatus of claim **1**, wherein the diffusion barrier is a narrow flow segment.

4. The apparatus of claim **1**, wherein the balloon has a substantially spherical shape when inflated.

5. The apparatus of claim **1**, wherein the balloon is secured to the catheter at substantially a single point on the balloon body.

6. The apparatus of claim **1**, wherein the balloon is secured to the catheter at a plurality of points on the balloon body.

7. The apparatus of claim **1**, wherein the catheter further comprises a malleable element.

8. The apparatus of claim **1**, wherein the balloon body is substantially impermeable to the treatment fluid.

9. The apparatus of claim **1**, wherein the balloon comprises a semipermeable membrane.

10. The apparatus of claim **1**, wherein the treatment fluid receptacle is sized and dimensioned for being flushed with a flushing fluid without substantially expanding the balloon.

11. The apparatus of claim **1**, wherein the balloon is secured to the catheter such that the balloon maintains a pre-selected shape during inflation.

12. The apparatus of claim **1**, wherein the balloon comprises a double-walled balloon having an inner wall and an outer wall.

13. The apparatus of claim **1**, wherein the balloon is sized and dimensioned for placement in a blood vessel.

14. The apparatus of claim **1**, wherein the balloon is sized and dimensioned for placement in a cavity left by surgical removal of a tumor from the patient.

15. The apparatus of claim **1**, wherein the balloon is sized and dimensioned for placement in a natural body cavity.

16. The apparatus of claim **1**, wherein the balloon is filled with a treatment fluid.

17. The apparatus of claim **16**, wherein the treatment fluid is a radioactive fluid.

18. The apparatus of claim **16**, wherein the treatment fluid has substantially physiological tonicity.

19. The apparatus of claim **12**, further comprising a second treatment fluid receptacle.

20. The apparatus of claim **19**, wherein the second treatment fluid receptacle fluidly communicates with a volume between inner and outer balloon walls.

21. An implantable apparatus for treating a proliferative disorder in a patient, comprising:

a treatment fluid receptacle for receiving a treatment fluid;

an inflatable balloon having a balloon body; and

a catheter connected between the treatment fluid receptacle and the balloon and defining a fluid flow path therebetween;

wherein the catheter further comprises a malleable element.

22. The apparatus of claim **21**, wherein the malleable element does not substantially interfere with NMR analysis.

23. The apparatus of claim **21**, wherein the balloon is sized and dimensioned for placement in a blood vessel.

24. An implantable apparatus for treating a proliferative disorder in a patient, comprising:

a treatment fluid receptacle for receiving a treatment fluid;

an inflatable balloon having a balloon body;

a catheter connected between the treatment fluid receptacle and the balloon and defining a fluid flow path therebetween; and

a diffusion barrier disposed in the fluid flow path between the treatment fluid receptacle and the balloon;

wherein the treatment fluid receptacle is adapted to be flushed with a small volume of a flush fluid.

25. A method for treating a proliferative disorder in a patient, the method comprising the steps of:

implanting in the patient's body an inflatable treatment apparatus, the apparatus comprising:

a treatment fluid receptacle for receiving a treatment fluid;

an inflatable balloon having a balloon body;

a catheter connected between the treatment fluid receptacle and the balloon and defining a fluid flow path therebetween; and

a diffusion barrier disposed in the fluid flow path between the treatment fluid receptacle and the balloon; and

introducing a treatment fluid into the treatment fluid receptacle such that the balloon is inflated;

such that the proliferative disorder is treated.

26. The method of claim **25**, further comprising the step of flushing the treatment fluid into the balloon.

27. The method of claim **25**, wherein the treatment fluid is flushed into the balloon with a flush fluid.

28. The method of claim **27** wherein the flush fluid further inflates the balloon by no more than **10%** of the balloon volume prior to the flushing step.

29. The method of claim **25**, wherein the implanting step comprises the step of positioning the inflatable balloon adjacent to a tumor.

30. The method of claim **29**, wherein the implanting step comprises the step of positioning the inflatable balloon adjacent to a solid tumor.

31. The method of claim **29**, wherein the implanting step comprises the step of positioning the inflatable balloon adjacent to a cancerous tumor.

32. The method of claim **29**, wherein the implanting step comprises the step of positioning the inflatable balloon adjacent to a brain tumor.

33. The method of claim **29**, wherein the implanting step comprises the step of positioning the inflatable balloon adjacent to a breast tumor.

34. The method of claim **25**, further comprising, prior to the implanting step, the step of surgically creating a cavity in the patient's body.

35. The method of claim **25**, further comprising, prior to the implanting step, the step of selecting a balloon for treating the proliferative disorder.

36. The method of claim **35**, further comprising, prior to the implanting step, the step of assembling the inflatable treatment apparatus.

37. The method of claim **25**, wherein the apparatus is implanted in a natural body cavity.

38. A method for treating a proliferative disorder in a patient, the method comprising:

determining a characteristic of a cavity in the patient's body, the characteristic being selected from the group consisting of volume, shape, or a dimension;

selecting an inflatable balloon suitable for placement in the cavity, the balloon including a balloon body;

implanting in the cavity an inflatable treatment apparatus comprising:

a treatment fluid receptacle for receiving a treatment fluid;

the inflatable balloon;

a catheter connected between the treatment fluid receptacle and the balloon and defining a fluid flow path therebetween;

a diffusion barrier disposed in the fluid flow path between the treatment fluid receptacle and the balloon; and

introducing a treatment fluid into the treatment fluid receptacle such that the balloon is inflated;

such that the proliferative disorder is treated.

39. The method of claim **38**, wherein the treatment fluid is a radioactive fluid.

40. The method of claim **38**, wherein the treatment fluid is a chemotherapy fluid.

41. The method of claim **38**, the method comprising, prior to the implanting step, the further step of assembling the inflatable treatment apparatus.

42. An implantable apparatus for treating a proliferative disorder in a patient, said apparatus comprising:

a treatment fluid receptacle for receiving a treatment fluid;

an inflatable balloon having a balloon body;

a catheter connected between said treatment fluid receptacle and said balloon, said catheter defining a fluid flow path therebetween; and

a narrow flow segment disposed in said fluid flow path between said treatment fluid receptacle and said balloon.

43. An implantable apparatus for treating a proliferative disorder in a patient, said apparatus comprising:

a treatment fluid receptacle for receiving a treatment fluid;

an inflatable balloon having a balloon body;

a catheter connected between said treatment fluid receptacle and said balloon, said catheter defining a fluid flow path therebetween;

a malleable element coupled to said catheter, and

a diffusion barrier disposed in the fluid flow path between said treatment fluid receptacle and said balloon.

* * * * *

Exhibit 41

CANACCORD Adams

Flash Update | 1

19 February 2008

SenoRx

SENO : NASDAQ : US$8.61

BUY

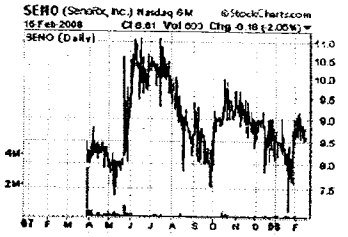
Target: US$12.25

Jason R. Mills 1.415.229.7166
jason.mills@canaccordadams.com
Jamar Ismail, CPA 1.415.229.0683
jamar.ismail@canaccordadams.com

COMPANY STATISTICS:

52-week Range:	US$7.1 - 11.10
Market Cap (M):	US$147.7
Shares Out (M):	17.1

SHARE PRICE PERFORMANCE:



COMPANY SUMMARY:

SenoRx designs, manufactures and markets minimally invasive medical devices used primarily in the diagnosis and treatment of breast cancer. Its core competency is percutaneous biopsy procedures, and its EnCor vacuum-assisted device for this market has many "pre-programmed" features, the TriCor concave tip, and a unique collection chamber. EnCor can be used with stereotactical (x-ray), ultrasound, and MRI imaging modalities.

All amounts in US$ unless otherwise noted.

DEPOSITION EXHIBIT
Davis 1
4-15-08

Life Sciences -- Biomedical Devices and Services

QUICK TAKE – STRONG Q4 REVENUE GROWTH CAPS OFF SOLID YEAR – MAINTAIN BUY RATING

Event

SenoRx reported Q4 results.

Action

We maintain our BUY rating.

Key points

Q4 revenue of $10.3M (+43% Y/Y) modestly beat our $10.2M estimate, led by strong biopsy disposable sales, which increased 43% versus our 42% growth expectation. Notably the company's revenue result for the year of $35.0M was at the high end of the $33-35M guidance that was originally given early in the year, post the march IPO. Hitting the top line is a notable achievement for a recently minted IPO company and gives us confidence that SenoRx can repeat that performance in 2008, especially with all the new product launches. We think top-line performance is the most important metric on which investors should focus at this point in the company's life cycle.

- SenoRx reiterated 2008 revenue guidance of $46-50M, which compares to our current estimate of $49.5M.
- SenoRx had penetrated 34 centers with its breast brachytherapy balloon Contura exiting 2007 versus our 20-center estimate; however, revenue associated with this penetration came in at about $300K versus our $900K estimate. Our checks have suggested in recent weeks that the company is supplying the early adopting centers – many of which are academic teaching institutions – with product at a lower price than what we think is the commercialized price (~$2,500-2,600).

Gross margin increased over 1,250bps Y/Y to 56% from 43.5%, albeit it was modestly lower than our 57.7% estimate as capital equipment revenue ($1.2M) doubled our estimate ($0.6M). Biopsy equipment revenues carry much lower GM than disposables and markers, while Contura balloon placements' below-market ASPs likely contributed as well.

Operating expenses totaling $8.7M significantly exceeded our $7.1M estimate as the company invested heavily in pre-launch sales and marketing resources ahead of full launch of Contura, VisiLoc and SenoSonix, all of which we expect to contribute meaningfully to growth in 2008.

- We are not at all concerned about the higher OpEx spending in the quarter; to wit, we think a company such as SenoRx in the earlier stages of a rapid growth trajectory should "strike while the iron is hot" in order to take advantage of growth opportunities in its key markets – namely breast cancer diagnosis and treatment.
- What's more, the company exited the quarter with $28M in cash, an untapped $4M credit facility and now virtually no long-term debt, owing to the retirement of a high-interest-rate loan facility in the quarter (11.5% interest rate) that consumed $10.3M in cash. In sum, we think the company is on solid financial footing.

Given the higher OpEx, partially offset by modestly higher revenue than we expected, the company reported GAAP net loss of $(0.23) per share versus our estimate of $(0.12)/share net loss.

We look forward to continued strong revenue growth and shrinking net loss for SenoRx in 2008. At this point we do not expect major changes to our current 2008 revenue and EPS estimates of $49.5M (+41.3%) and $(0.13), respectively.

We reiterate our BUY rating. Our price target is currently $12.25/share based on 4.0x EV/2008E sales of $49.5M. We will have more after the company's conference call, which will be conducted later today.

Investment risks

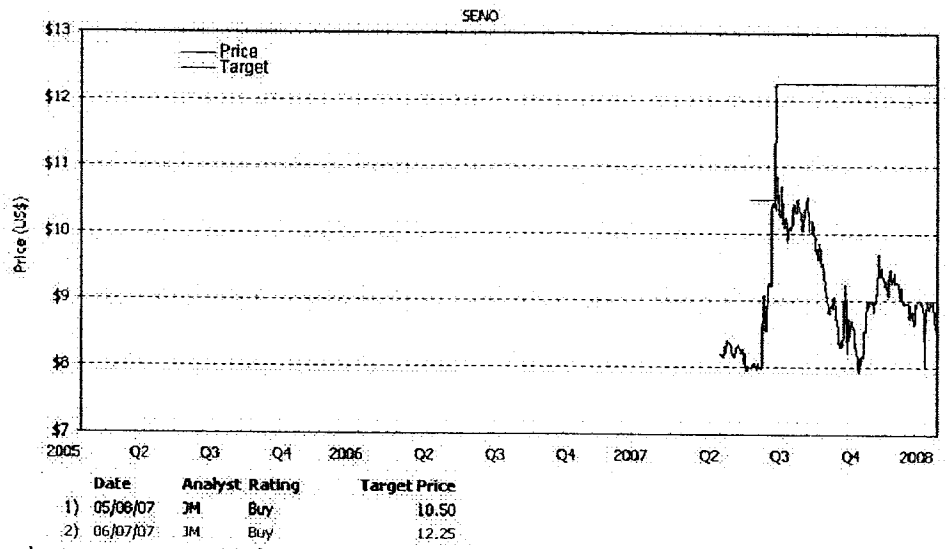
Financial and distribution strength of VAB biopsy competitors, uncertainty over which technology will "win" in breast brachytherapy, increased use of MRI and ultrasound, reimbursement and potential for pricing erosion.

APPENDIX: IMPORTANT DISCLOSURES

Analyst Certification: Each authoring analyst of Canaccord Adams whose name appears on the front page of this investment research hereby certifies that (i) the recommendations and opinions expressed in this investment research accurately reflect the authoring analyst's personal, independent and objective views about any and all of the designated investments or relevant issuers discussed herein that are within such authoring analyst's coverage universe and (ii) no part of the authoring analyst's compensation was, is, or will be, directly or indirectly, related to the specific recommendations or views expressed by the authoring analyst in the investment research.

Site Visit: An analyst has visited the issuer's material operations in Aliso Viejo, California. No payment or reimbursement was received from the issuer for the related travel costs.

Price Chart:*



	Date	Analyst	Rating	Target Price
1)	05/08/07	JM	Buy	10.50
2)	06/07/07	JM	Buy	12.25

* Price charts assume event 1 indicates initiation of coverage or the beginning of the measurement period.

Distribution of Ratings:
Global Stock Ratings
(as of 1 February 2008)

	Coverage Universe		IB Clients
Rating	#	%	%
Buy	313	60.3%	43.1%
Speculative Buy	62	11.9%	71.0%
Hold	128	24.7%	24.2%
Sell	16	3.1%	6.3%
	519	100.0%	

Canaccord Ratings System:

BUY: The stock is expected to generate risk-adjusted returns of over 10% during the next 12 months.
HOLD: The stock is expected to generate risk-adjusted returns of 0-10% during the next 12 months.
SELL: The stock is expected to generate negative risk-adjusted returns during the next 12 months.
NOT RATED: Canaccord Adams does not provide research coverage of the relevant issuer.

"Risk-adjusted return" refers to the expected return in relation to the amount of risk associated with the designated investment or the relevant issuer.

Risk Qualifier: SPECULATIVE: Stocks bear significantly higher risk that typically cannot be valued by normal fundamental criteria. Investments in the stock may result in material loss.

Canaccord Adams Research Disclosures as of 19 February 2008

Company	Disclosure
SenoRx	1A, 2, 3, 5, 7

1	The relevant issuer currently is, or in the past 12 months was, a client of Canaccord Adams or its affiliated companies. During this period, Canaccord Adams or its affiliated companies provided the following services to the relevant issuer: A. investment banking services. B. non-investment banking securities-related services. C. non-securities related services.
2	In the past 12 months, Canaccord Adams or its affiliated companies have received compensation for Corporate Finance/Investment Banking services from the relevant issuer.
3	In the past 12 months, Canaccord Adams or any of its affiliated companies have been lead manager, co-lead manager or co-manager of a public offering of securities of the relevant issuer or any publicly disclosed offer of securities of the relevant issuer or in any related derivatives.
4	Canaccord Adams acts as corporate broker for the relevant issuer and/or Canaccord Adams or any of its affiliated companies may have an agreement with the relevant issuer relating to the provision of Corporate Finance/Investment Banking services.
5	Canaccord Adams or any of its affiliated companies is a market maker or liquidity provider in the securities of the relevant issuer or in any related derivatives.
6	In the past 12 months, Canaccord Adams, its partners, affiliated companies, officers or directors, or any authoring analyst involved in the preparation of this investment research has provided services to the relevant issuer for remuneration, other than normal course investment advisory or trade execution services.
7	Canaccord Adams intends to seek or expects to receive compensation for Corporate Finance/Investment Banking services from the relevant issuer in the next six months.
8	The authoring analyst, a member of the authoring analyst's household, or any individual directly involved in the preparation of this investment research, has a long position in the shares or derivatives, or has any other financial interest in the relevant issuer, the value of which increases as the value of the underlying equity increases.
9	The authoring analyst, a member of the authoring analyst's household, or any individual directly involved in the preparation of this investment research, has a short position in the shares or derivatives, or has any other financial interest in the relevant issuer, the value of which increases as the value of the underlying equity decreases.
10	Those persons identified as the author(s) of this investment research, or any individual involved in the preparation of this investment research, have purchased/received shares in the relevant issuer prior to a public offering of those shares, and such person's name and details are disclosed above.
11	A partner, director, officer, employee or agent of Canaccord Adams and its affiliated companies, or a member of his/her household, is an officer, or director, or serves as an advisor or board member of the relevant issuer and/or one of its subsidiaries, and such person's name is disclosed above.
12	As of the month end immediately preceding the date of publication of this investment research, or the prior month end if publication is within 10 days following a month end, Canaccord Adams or its affiliate companies, in the aggregate, beneficially owned 1% or more of any class of the total issued share capital or other common equity securities of the relevant issuer or held any other financial interests in the relevant issuer which are significant in relation to the investment research (as disclosed above).
13	As of the month end immediately preceding the date of publication of this investment research, or the prior month end if publication is within 10 days following a month end, the relevant issuer owned 1% or more of any class of the total issued share capital in Canaccord Adams or any of its affiliated companies.
14	Other specific disclosures as described above.

Canaccord Adams is the business name used by certain subsidiaries of Canaccord Capital Inc., including Canaccord Adams Inc., Canaccord Adams Limited, and Canaccord Adams, a division of Canaccord Capital Corporation. Clients of Canaccord Adams, in the past 12 months, may have been clients of Canaccord Capital Corporation, Canaccord Capital (Europe) Limited, Canaccord Capital Corporation USA Inc., and/or Adams Harkness Financial Group Ltd.

The authoring analysts who are responsible for the preparation of this investment research are employed by Canaccord Adams, a securities broker-dealer with principal offices located in Vancouver, Calgary, Toronto, Montreal (all Canada), Boston, New York, San Francisco (all US) and London (UK).

In the event that this is compendium investment research (covering six or more relevant issuers), Canaccord Adams and its affiliated companies may choose to provide specific disclosures of the subject companies by reference, as well as its policies and procedures regarding the dissemination of investment research. To access this material or for more information, please send a request to Canaccord Adams Research, Attn: Disclosures, P.O. Box 10337 Pacific Centre, 2200-609 Granville Street, Vancouver, BC, Canada V7Y 1H2 or disclosures@canaccordadams.com.

The authoring analysts who are responsible for the preparation of this investment research have received (or will receive) compensation based upon (among other factors) the Corporate Finance/Investment Banking

revenues and general profits of Canaccord Adams. However, such authoring analysts have not received, and will not receive, compensation that is directly based upon or linked to one or more specific Corporate Finance/Investment Banking activities, or to recommendations contained in the investment research.

Canaccord Adams and its affiliated companies may have a Corporate Finance/Investment Banking or other relationship with the company that is the subject of this investment research and may trade in any of the designated investments mentioned herein either for their own account or the accounts of their customers, in good faith or in the normal course of market making. Accordingly, Canaccord Adams or their affiliated companies, principals or employees (other than the authoring analyst(s) who prepared this investment research) may at any time have a long or short position in any such designated investments, Related designated investments or in options, futures or other derivative instruments based thereon.

Some regulators require that a firm must establish, implement and make available a policy for managing conflicts of interest arising as a result of publication or distribution of investment research. This investment research has been prepared in accordance with Canaccord Adams' policy on managing conflicts of interest, and information barriers or firewalls have been used where appropriate. Canaccord Adams' policy is available upon request.

The information contained in this investment research has been compiled by Canaccord Adams from sources believed to be reliable, but (with the exception of the information about Canaccord Adams) no representation or warranty, express or implied, is made by Canaccord Adams, its affiliated companies or any other person as to its fairness, accuracy, completeness or correctness. Canaccord Adams has not independently verified the facts, assumptions, and estimates contained herein. All estimates, opinions and other information contained in this investment research constitute Canaccord Adams' judgement as of the date of this investment research, are subject to change without notice and are provided in good faith but without legal responsibility or liability.

Canaccord Adams salespeople, traders, and other professionals may provide oral or written market commentary or trading strategies to our clients and our proprietary trading desk that reflect opinions that are contrary to the opinions expressed in this investment research. Canaccord Adams' affiliates, proprietary trading desk, and investing businesses may make investment decisions that are inconsistent with the recommendations or views expressed in this investment research.

This investment research is provided for information purposes only and does not constitute an offer or solicitation to buy or sell any designated investments discussed herein in any jurisdiction where such offer or solicitation would be prohibited. As a result, the designated investments discussed in this investment research may not be eligible for sale in some jurisdictions. This investment research is not, and under no circumstances should be construed as, a solicitation to act as a securities broker or dealer in any jurisdiction by any person or company that is not legally permitted to carry on the business of a securities broker or dealer in that jurisdiction. This material is prepared for general circulation to clients and does not have regard to the investment objectives, financial situation or particular needs of any particular person. Investors should obtain advice based on their own individual circumstances before making an investment decision. To the fullest extent permitted by law, none of Canaccord Adams, its affiliated companies or any other person accepts any liability whatsoever for any direct or consequential loss arising from or relating to any use of the information contained in this investment research.

For Canadian Residents: This Investment Research has been approved by Canaccord Adams, a division of Canaccord Capital Corporation, which accepts responsibility for this Investment Research and its dissemination in Canada. Canadian clients wishing to effect transactions in any Designated Investment discussed should do so through a qualified salesperson of Canaccord Adams, a division of Canaccord Capital Corporation in their particular jurisdiction.

For United Kingdom Residents: This Investment Research complies with of the Financial Services Authority's Handbook's chapter on Conduct of Business and is approved by Canaccord Adams Limited, which is regulated and authorized by the Financial Services Authority, in connection with its distribution in the United Kingdom. This material is not for distribution in the United Kingdom to private customers, as defined under the rules of the Financial Services Authority. Canaccord Adams Limited accepts responsibility for this Investment Research and its dissemination in the United Kingdom. The information contained in this Investment Research is only intended for distribution in the UK to persons who qualify as intermediate customers or market counterparties, as defined under the rules of the Financial Services Authority.

For United States Residents: Canaccord Adams Inc., a US registered broker-dealer, accepts responsibility for this Investment Research and its dissemination in the United States. This Investment Research is intended for distribution in the United States only to certain US institutional investors. US clients wishing to effect transactions in any Designated Investment discussed should do so through a qualified salesperson of Canaccord Adams Inc.

For European Residents: If this Investment Research is intended for disclosure in any jurisdiction other than the United Kingdom, the US or Canada, then the relevant rules and regulatory requirements of that jurisdiction will apply.

Additional information is available on request.

ocument

CANACCORD Adams

Daily Letter | 1
20 February 2008

SenoRx

SENO : NASDAQ : US$8.64

BUY

Target: US$12.25

Jason R. Mills 1.415.229.7166
jason.mills@canaccordadams.com
Jamar Ismail, CPA 1.415.229.0683
jamar.ismail@canaccordadams.com

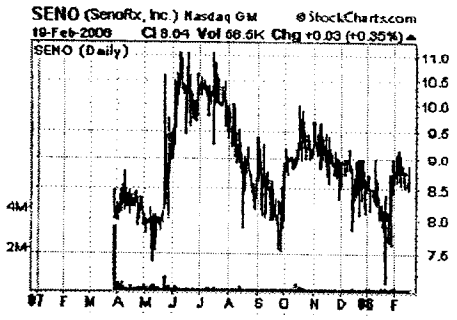
COMPANY STATISTICS:

52-week Range:	US$7.10 - 11.10
Market Cap (M):	US$147.7
Shares Out (M):	17.1

EARNINGS SUMMARY:

FYE Dec		2007A	2008E	2009E
Revenue (M):		35.0	49.5	67.2
EPS:		(0.59)	(0.28)	0.23
Revenue (M):	Q1	7.7	10.7	-
	Q2	8.1	11.7	-
	Q3	8.9	12.5	-
	Q4	10.3	14.6	-
Total		35.0	49.5	67.2
EPS:	Q1	(0.20)	(0.12)	-
	Q2	(0.15)	(0.09)	-
	Q3	(0.10)	(0.06)	-
	Q4	(0.16)	(0.01)	-
Total		(0.59)	(0.28)	0.23

SHARE PRICE PERFORMANCE:



COMPANY SUMMARY:

SenoRx designs, manufactures and markets minimally invasive medical devices used primarily in the diagnosis and treatment of breast cancer. Its core competency is percutaneous biopsy procedures, and its EnCor vacuum-assisted device for this market has many "pre-programmed" features, the TriCor concave tip, and a unique collection chamber. EnCor can be used with stereotactical (x-ray), ultrasound, and MRI imaging modalities.

All amounts in US$ unless otherwise noted.

Life Sciences -- Biomedical Devices and Services

SOLID Q4 – MAINTAIN BUY RATING

Event

SenoRx reported Q4 results highlighted by strong revenue growth.

Action

We maintain our BUY rating and $12.25 price target

Key points

Q4 revenue of $10.3M (+43% Y/Y) modestly beat our/consensus $10.2M estimate. Notably 2007 revenue of $35.0M hit the high end of $33-35M guidance originally given after its March IPO. Pro-forma EPS of $(0.16) compared to our $(0.05) estimate, driven by higher spending to support product launches and add sales reps – a strategy we believe is best to sustain strong growth. Gross margin increased over 1,250bps Y/Y to 56.0% from 43.5%, albeit modestly lower than our Q4 estimate.

Revenue growth was led by strong biopsy disposable sales, which increased 43% versus our 42% growth expectation, and system revenue of $1.1M doubled our estimate. Adjunct sales (Markers & Gamma detection) were $4.1M and Contura sales were $0.3M.

Encore placements in Q4 were very strong at 80 units and represent a strong leading indicator of future disposable sales. Importantly, SEMP estimated its current VAB disposables market share is 15%, while current share of new system placements eclipses 35%. We view this disparity as a favorable signal that biopsy disposable growth can continue to grow robustly – perhaps higher than our 2008 estimates.

SenoRx reiterated 2008 revenue guidance of $46-50M. We maintain our $49.5M estimate (+41% Y/Y), albeit we widen our net loss/share estimate to $(0.28) from $(0.12) as we expect SenoRx to "strike while the iron is hot" to further develop core growth markets and continue to gain share.

We reiterate our BUY rating and $12.25 target (4x our 2008E sales).

Bottom line – We suggest SenoRx possesses scarcity value within a consolidating breast device space that we think could justify a premium valuation. Reflecting conservatism, however, our $12.25 target reflects an EV/Sales multiple of 4.0x, which is a 22% discount to the small-cap med-tech comparable group multiple of 5.1x. We apply this 4.0x multiple to our 2008 sales estimate of $49.5 million to derive our 12-month price target.

DISCUSSION

SenoRx reported Q4/07 revenue of $10.3M (+43% Y/Y) modestly beating our and consensus estimates of $10.2M. Operating loss was $2.9M and pro-forma net loss per share was $(0.16), compared to an operating loss of $3.2M in Q4/06. This was below our estimate for operating loss of $1.2M and net loss per share of $(0.05) and below consensus net loss per share of $(0.10). GAAP net loss per share of $(0.23) includes $1.1M of expenses related to the early extinguishment of debt.

Notably the company's revenue result for the year of $35.0M was at the high end of the $33-35M guidance that was originally given early in the year post the March IPO. We think this top-line result relative to guidance and consensus is a notable achievement for a recently minted IPO company and gives us confidence that the company can repeat this strong performance in 2008, especially given several new product launches – Contura MLB, VisiLoc and SenoSonix system. We continue to recommend investors focus on the top-line performance, which we think is the most important metric to watch at this early point in the company's life cycle.

Revenue by segment:

- Revenue growth was led by strong biopsy disposable sales of $4.7M (+43% Y/Y) slightly better than our expectation of $4.6M (+42% Y/Y).
- Placements were very strong. Equipment revenue was $1.1M (+Y/Y), vs. our expectation of $0.6M. Total EnCor system placements were 80 units, up from 50 in Q3/07, 45 in Q4/06 and higher than our estimate of 51. Cumulative systems reached 536 at the end of 2007, up from 317 at the end of 2006. Given that laser placements represent a leading indicator of the ultra-important disposable EnCor biopsy sales in this prototypical razor/razor-blade model, we submit that the stronger system placements in Q4 – and previously in Q3 as well – give us increasing confidence in strong 2008 disposables sales. Importantly, management estimates that its current market share of disposables is 15%, while current share of new system placements is greater than 35%, owing to momentum over the past year. We think this represents a positive signal for SenoRx, and suggests to us that biopsy disposable growth should continue to exhibit strong growth in 2008 – perhaps higher than our current model, which calls for biopsy disposables sales growth of 39.1% Y/Y.
- Diagnostic adjunct sales (Markers & Gamma detection) were $4.1M (+ Y/Y), matching our estimate.
- Contura sales were $329K vs. our estimate of $900K. SenoRx had penetrated 34 centers with its breast brachytherapy balloon Contura exiting 2007 versus our 20-center estimate; however, revenue associated with this penetration came in lower than expected. Our checks have suggested in recent weeks that the company is supplying the early adopting centers – many of which are academic teaching institutions – with product at no charge. Additionally, in the early stages of this launch the company in

some instances had to swap out existing inventory of competitor product and/or pay re-stocking fees up to 20%, both of which counted against average ASPs for Contura in the quarter. We think these "offsets" will decline throughout 2008, and continue to see the company achieving an average ASP – all things being equal – in the $2500-2700 range in H2/2008 and 2009.

Gross margin increased over 1,250bps Y/Y to 56.0% from 43.5%, albeit were modestly lower than our 57.7% estimate, owing to 1) lower-margin capital equipment revenue doubling our estimate (about 1/3 of the shortfall, according to management), 2) higher international sales which are also lower margin relative to domestic sales, and 3) re-valuation of inventory via the shift of the rest of its manufacturing overseas to Thailand, including increasing its obsolescence reserve because of discontinuation of Anchor Guide (this resulted in 1.5% of the shortfall and WILL NOT recur).

We see significant gross margin expansion going forward, with our model for GM increasing sequentially in 2008 and reaching 64.4% exiting the year. We model GM of 61.8% for the full year 2008 and 66% in 2009 driven by increased disposable sales and additional manufacturing efficiencies.

Operating expenses totaling $8.7M significantly exceeded our $7.1M estimate as the company invested heavily in pre-launch sales and marketing resources ahead of full launch of Contura, VisiLoc and SenoSonix, all of which we expect to contribute meaningfully to growth in 2008.

- We are not at all concerned about the higher OpEx spending in the quarter; to wit, we think a company such as SenoRx in the earlier stages of a rapid growth trajectory should "strike while the iron is hot" in order to take advantage of growth opportunities in its key markets – namely breast cancer diagnosis and treatment.
- What's more, the company exited the quarter with $28M in cash; an untapped $4M credit facility and now virtually no long-term debt, owing to the retirement of a high interest rate loan facility in the quarter (11.5% interest rate) that consumed $10.3M in cash. In sum, we think the company is on solid financial footing.

Given the higher OpEx, partially offset by modestly higher revenue than we expected, the company reported pro-forma loss per share of $(0.16) vs. our estimate of $(0.05). GAAP net loss per share was $0.23 v. our estimate of $0.12/share net loss.

SenoRx reiterated 2008 revenue guidance of $46-50M, which compares to our current estimate of $49.5M and consensus of $49.9M.

Estimate changes. For 2008 we are keeping our revenue estimate at $49.5M (+41.4%) and widening our loss per share estimate to $(0.28) from $(0.12) to account for increased product launch expenses and $1.4-$1.7M in incremental legal expenses associated with litigation to defend itself against a lawsuit recently brought by Hologic regarding Contura. For 2009 we are maintaining our estimates of revenue of $67.2M and EPS of $0.23. We think the company can turn EBITDA positive in Q4/08 or Q1/09.

Product initiative update

Contura – The company initiated full US commercial launch in January. Q4/07 revenue was lower than expected but as we mentioned earlier our checks suggest that the company has been offering product to teaching medical centers at a discount. The company expects some of these centers to begin publishing abstracts soon. Positive data – especially data that suggests the multi-lumen aspect of Contura will allow more patients to be treated – are key to adoption and market expansion. We have tempered our revenue expectation for 2008 and now see a $6M contribution from Contura for the year versus our previous estimate of $7.5M, as we expect continued impact in H1/2008 from the teaching hospital placements, re-stocking fees and inventory swap charges noted earlier.

VisiLoc – This extension to the EnCor system was FDA 510k approved in November 2007. The VisiLoc MRI Visible Obturator allows for more precise location of the target tumor in MRI assisted breast biopsy. We think VisiLoc could be an important differentiator of the Encor platform, and could help SenoRx grab even more share of the vacuum assisted biopsy market, especially if/as procedures move toward MRI relative to stereotactic guidance.

SenoSonix – This combination biopsy/ultrasound device was FDA 510K approved in October 2007 and the company has initiated a launch in the US office segment. We do not model significant revenue from this segment. European launch will be more significant, in our view, as European physicians perform a higher percentage of ultrasound guided biopsies. The company expects to receive CE Mark this quarter.

Training and Sales Force. The company continues to spend on educational seminars and conducted a total of 64 in 2007 during which ~1,355 doctors were trained on SenoRx products. This initiative will continue in 2008 and will include seminars focused on Contura. In addition the company continued to add to its US and international sales infrastructure – including 5 brachytherapy specialists – which we also expect to continue to grow in 2008 and 2009.

- Sales force expansion is important to growth, in our view. SenoRx significantly expanded its direct US sales force in 2006 on the heels of the EnCor biopsy system launch in late 2005, and this expansion continued in 2007, including the addition of a five brachytherapy sales specialist group, whose expertise should be valuable in marketing SenoRx's proprietary Radiation Balloon to surgeons and radiation-oncologists. In total, SenoRx exited 2007 with a direct sales organization totaling 65, including 47 quota-carrying reps and nearly 20 clinical specialists. We expect the sales force additions to continue in 2008. The company is also taking steps to expand and bolster its OUS direct and distributor sales force

Investment thesis

We are maintaining our Buy rating and $12.25 price target. We think that this was a solid quarter to end a solid year for SenoRx. Positives include continued strong biopsy disposable sales growth of 42% as the company gains market share, impressive and accelerating EnCor system placements which bode well for future disposable growth and gross margin expansion Y/Y that we expect to continue – if not accelerate – going forward. Operating expenses were higher than expected, but sensible given that the company is still developing markets, gaining share and launching new products in new markets.

In essence, we "buy into" the strategy of "striking while the iron is hot" as opposed to "starving the business" in favor of modest earnings or lower net losses. We have seen the former strategy work before in small-cap med-tech – including Spectranetics, which decided to develop the PAD market and strive for share gain in this market, successfully we might add – over the past half decade, during which time the stock has more than quintupled from its lows in 2003.

SenoRx is unique in that it is the only independent company that possesses next-generation devices that address the entire continuum of care in breast cancer: diagnosis/biopsy, marking, excision and treatment solutions. We view the minimally invasive biopsy and breast brachytherapy opportunities as particularly attractive as long-term growth markets in the medical device arena.

Minimally invasive biopsy and breast brachytherapy opportunities are particularly attractive to us. We estimate the percutaneous vacuum-assisted biopsy market at $195.3 million in 2007, with growth of about 15% per annum. We project growth in the number of ultrasound-guided vacuum-assisted biopsies could approximate 17.4% (2005-2009) and note that this could be conservative as a result of the aforementioned drivers for ultrasound usage in general. SenoRx's EnCor vacuum-assisted biopsy system is state-of-the art, and we expect sales gains for this system to exceed market growth handily over our forecast period. The breast brachytherapy market is nascent at only $44.3 million estimated for 2007 but expected to grow robustly over a five year period. Contura, the company's multi-lumen radiation balloon for breast brachytherapy, is in the initial stages of its full commercial launch and we expect a steep revenue ramp beginning in 2008.

Classic "triple-play" med-tech growth story. SenoRx has driven impressive revenue growth and product innovation since its inception in 1998. We think the best days are ahead of the company owing to what we identify as a classic "triple-play" small-cap company growth formula, namely: 1) differentiated technology addressing attractive segments of a growth market (in this case the breast device market), 2) strong R&D culture that has produced a strong new product pipeline, and 3) ramping direct sales force.

Contura could be a major catalyst for SenoRx, as well as the localized radiation therapy market as a whole in coming years. We believe SenoRx's device surpasses the capabilities of and addresses a larger patient population than other localized brachytherapy devices. It is the only multi-lumen balloon therapy on the market (more precise targeting and possibly higher reimbursement) and its "on-board" vacuum and proprietary balloon material add to its efficacy and differentiation, in our view.

Strong product pipeline. The fruits of the company's strong R&D culture seem poised to bear additional fruit in the coming months and years. In addition to Contura, the company plans several additional sizes and iterations during 2008, with the European launch of SenoSonix also expected soon. Also, we expect SenoRx to introduce two innovative breast excision devices (Single Step and Shape Select) in 2009. We think the Single Step – which has already received FDA 510k clearance – could fulfill an unmet need for surgeons, as well as potentially acting as an adjunct driver of Contura sales, as it creates a "smooth" lesion cavity for enhanced placement of these balloon catheters. The Shape Select, also FDA-cleared, is designed for use in reconstructive breast procedures. We also look forward to the introduction of a cordless model in the EnCor family, which we think will be popular with physicians and OR staffs. Lastly, we expect the company to continue expanding its market-leading marker portfolio over the next two years.

Valuation

The broad small-cap med-tech comp group (composed of over 60 companies with market caps under $1.5 billion) currently trades at a mean EV/ sales multiple of 5.1x (excluding high and low outliers) relative to C2007E revenue. SenoRx' 2007 revenue grew to $35 million, representing an increase of 37% versus 2006 levels and we project it to grow to $49.5M in 2008 representing a 41.4% Y/Y increase. While this revenue growth is strong and could justify an in-line or even premium multiple relative to the comp group, we choose to apply a 22% discount to the group average (reflecting conservatism perhaps) to derive a target EV/Sales multiple of 4.0x, which we apply to our $49.5M 2008 sales estimate to derive our price target of $12.25/share 12 months hence.

Figure 1: Matrix of discount rates and implied share price target

		Discount to Comp Group		
		17%	22%	27%
Target EV/Sales multiple for SENO common		4.2x	4.0x	3.7x
Implied Price Target on SENO common		$12.94	$12.25	$11.55
Financial Metrics Used in Analysis				
Broad small-cap medical device EV/Sales multiple (C2007E)	5.1x			
SENO 2008E Sales ($ mil)	$49.5			
Cash ($ mil)	$28			
Debt ($ mil)	$2			
Diluted shares outstanding (mil)	18			

Source: Canaccord Adams.

Investment risks

Financial and distribution strength of VAB biopsy competitors, uncertainty over which technology will "win" in breast brachytherapy, increased use of MRI and ultrasound, reimbursement and potential for pricing erosion.

Figure 2: Quarterly income statement

INCOME STATEMENT
Fiscal Year End - Dec
($mil - except per share data)

	CY 2004	CY 2005	CY 2006	2007 Mar	2007 Jun	2007 Sep	2007 Dec	CY 2007	2008E MarE	2008E JunE	2008E SepE	2008E DecE	CY 2008E	CY 2009E
Total revenue	$ 13.8	$ 19.3	$ 25.5	$ 7.7	$ 8.1	$ 8.9	$ 10.3	$ 35.0	$ 10.7	$ 11.7	$ 12.5	$ 14.6	$ 49.5	$ 67.2
Cost of goods sold	6.4	10.1	13.5	3.5	3.5	3.6	4.5	15.1	4.4	4.6	4.7	5.2	18.9	22.8
Gross profit	7.3	9.1	12.0	4.2	4.6	5.4	5.8	19.9	6.3	7.1	7.8	9.4	30.6	44.4
R&D (including options exp)	4.8	4.9	5.3	1.5	1.6	1.6	1.7	6.4	1.7	1.8	1.9	1.9	7.2	8.1
Selling & marketing (incl. option	7.5	10.1	15.0	4.3	4.4	4.4	5.9	19.0	6.0	6.1	6.1	6.6	24.8	27.7
G&A (incl. options)	1.7	2.1	2.0	0.8	1.1	1.2	1.1	4.2	1.1	1.1	1.2	1.3	4.6	5.4
Operating income/(Loss)	(6.7)	(8.0)	(10.4)	(2.4)	(2.6)	(1.8)	(2.9)	(9.6)	(2.5)	(1.9)	(1.3)	(0.4)	(6.1)	3.2
Other, net	0.0	0.1	0.1	0.8	0.3		-	1.1	-	-	-	-	-	-
Net interest income/(expense)	(0.2)	(0.7)	(1.0)	(0.5)	0.1	0.1	0.2	(0.1)	0.3	0.3	0.2	0.3	1.0	1.0
Pretax income	(6.8)	(8.6)	(11.3)	(2.1)	(2.1)	(1.7)	(2.7)	(8.7)	(2.2)	(1.6)	(1.1)	(0.2)	(5.1)	4.2
Tax expense	0.1	0.0	-	-	-	-	-	-	-	-	-	-	-	-
Tax Rate	n/a	n/a	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
Net income/(loss) - Pro forma	(6.9)	(8.6)	(11.3)	(2.1)	(2.1)	(1.7)	(2.7)	(8.7)	(2.2)	(1.6)	(1.1)	(0.2)	(5.1)	4.2
Extraordinary charges (net of tax)			(4.1)				(1.3)	(1.3)						
Net income/(loss) - GAAP	(6.9)	(8.6)	(15.4)	(2.1)	(2.1)	(1.7)	(4.0)	(9.9)	(2.2)	(1.6)	(1.1)	(0.2)	(5.1)	4.2
Shares outstanding	17.8	17.8	17.8	10.7	13.9	17.1	17.2	14.7	17.6	17.8	17.9	18.1	17.8	18.2
EPS - Pro forma	$ (0.39)	$ (0.48)	$ (0.63)	$ (0.20)	$ (0.15)	$ (0.10)	$ (0.16)	$ (0.59)	$ (0.12)	$ (0.09)	$ (0.06)	$ (0.01)	$ (0.28)	$ 0.23
EPS - GAAP	$ -	$ -	$ 6.51	$ (0.20)	$ (0.15)	$ (0.10)	$ (0.23)	$ (0.68)	$ (0.12)	$ (0.09)	$ (0.06)	$ (0.01)	$ (0.28)	$ 0.23
Margin Analysis														
Gross Margin	53.3%	47.5%	47.1%	54.1%	57.0%	60.1%	56.0%	56.8%	58.9%	60.5%	62.5%	64.4%	61.8%	66.0%
Operating Margin	-48.5%	-41.6%	-40.8%	-31.0%	-31.4%	-20.1%	-28.3%	-27.5%	-23.0%	-15.9%	-10.7%	-2.9%	-12.3%	4.8%
Pretax Margin	-49.6%	-44.7%	-44.1%	-27.4%	-26.3%	-19.0%	-26.5%	-24.7%	-20.4%	-13.7%	-8.8%	-1.1%	-10.2%	6.3%
Net Margin	-50.1%	-44.8%	-44.1%	-27.4%	-26.3%	-19.0%	-26.5%	-24.7%	-20.4%	-13.7%	-8.8%	-1.1%	-10.2%	6.3%
R & D - % Revenue	34.8%	25.5%	20.9%	19.1%	20.3%	17.7%	16.1%	18.1%	15.9%	15.5%	14.8%	12.8%	14.6%	12.0%
Selling & Marketing - % Revenue	54.6%	52.7%	59.0%	55.8%	54.6%	48.9%	57.6%	54.3%	56.0%	51.6%	49.0%	45.5%	50.1%	41.2%
G & A - % Revenue	12.4%	11.0%	8.0%	10.2%	13.6%	13.5%	10.6%	11.9%	10.0%	9.4%	9.4%	9.0%	9.4%	8.0%
Growth (Y/Y)														
Revenue	n/a	40.0%	32.5%	32.0%	28.4%	45.0%	43.1%	37.4%	39.0%	44.5%	40.7%	41.3%	41.4%	35.8%
COGS	n/a	57.5%	33.6%	14.6%	14.3%	7.7%	11.7%	12.0%	24.3%	32.8%	32.1%	14.1%	25.0%	20.7%
Gross Income	n/a	24.7%	31.2%	51.5%	41.5%	88.1%	83.9%	65.9%	51.4%	53.3%	46.3%	62.7%	53.8%	45.0%
Operating Income	n/a	20.2%	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Net Income	n/a	125.2%	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
EPS	n/a	125.2%	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a

Source: Company reports and Canaccord Adams estimates

Figure 3: Revenues by segment

REVENUE MODEL

	CY 2004	CY 2005	CY 2006	2007 Mar	2007 Jun	2007 Sep	2007 Dec	CY 2007	2008E MarE	2008E JunE	2008E SepE	2008E DecE	CY 2008E	CY 2009E
Unit Model														
Disposables														
EnCor Biopsy	4,693	24,183	44,829	14,446	16,628	16,378	19,180	66,632	20,369	23,445	22,913	26,823	93,551	121,420
SenoCor Biopsy	3,333	3,333	3,823	997	1,095	995	1,212	4,300	1,132	1,243	1,129	1,376	4,880	5,466
Units - Total Biopsy	8,026	27,516	48,652	15,443	17,723	17,372	20,393	70,932	21,501	24,689	24,042	28,200	98,431	126,886
Captive Markers	19,546	26,817	35,575	13,650	14,363	16,490	19,106	63,609	19,383	20,036	22,674	24,838	86,931	112,275
Non-Captive Markers	119,718	119,718	124,300	32,652	31,200	30,792	32,640	127,285	33,632	32,136	31,716	33,619	131,103	133,856
Units - Total Markers	139,265	146,535	163,875	46,302	45,563	47,282	51,746	190,893	53,015	52,172	54,390	58,457	218,034	246,131
Single Step	-	-	-	-	-	-	-	-	-	-	250	250	500	3,250
Shape Select	-	-	-	-	-	-	-	-	-	-	250	300	550	3,150
Anchor Guide	1,128	1,343	775	200	140	200	200	740	-	-	-	-	-	-
Contura radiation balloon therapy	-	-	-	-	10	71	195	276	341	456	661	935	2,392	5,375
OED	-	-	-	-	-	-	-	-	-	-	-	-	-	500
Gamma Detection	72	56	82	21	11	20	24	75	27	27	28	29	111	130
Capital Equipment								-					-	-
EnCor Biopsy Equipment Sold	89	89	60	24	30	40	50	144	39	39	38	38	154	135
SenoCor Biopsy Equipment PBA	30	30	89	19	16	10	30	75	16	16	16	20	68	82
Units - EnCor Biopsy Equipment Total	119	119	149	43	46	50	80	219	55	55	54	58	222	217
Units - SenoCor Biopsy Equipment	7	7	3	1	1	1	1	4	1	1	1	1	4	4
Average Selling Prices														
EnCor Biopsy	$ 240	$ 230	$ 230	$ 230	$ 230	$ 230	$ 230	$ 230	$ 230	$ 230	$ 230	$ 230	$ 230	$ 230
SenoCor Biopsy	$ 180	$ 180	$ 180	$ 180	$ 180	$ 180	$ 180	$ 180	$ 180	$ 180	$ 180	$ 180	$ 180	$ 180
Captive Markers	$ 71	$ 71	$ 71	$ 71	$ 71	$ 71	$ 71	$ 71	$ 71	$ 71	$ 71	$ 71	$ 71	$ 71
Non-captive Markers	$ 71	$ 71	$ 71	$ 71	$ 71	$ 71	$ 71	$ 71	$ 71	$ 71	$ 71	$ 71	$ 71	$ 71
EnCor Biopsy Equipment Sold	$ 20,500	$ 20,500	$ 19,281	$ 20,000	$ 20,097	$ 25,289	$ 23,550	$ 22,234	$ 22,000	$ 22,000	$ 22,000	$ 22,000	$ 22,000	$ 21,000
SenoCor Biopsy Equipment	$ 17,500	$ 17,500	$ 17,500	$ 17,500	$ 17,500	$ 17,500	$ 17,500	$ 17,500	$ 17,500	$ 17,500	$ 17,500	$ 17,500	$ 17,500	$ 17,500
Single Step	$ 300	$ 300	$ 300	$ 300	$ 300	$ 300	$ 300	$ 300	$ 300	$ 300	$ 300	$ 300	$ 300	$ 300
Shape Select	$ 100	$ 100	$ 100	$ 100	$ 100	$ 100	$ 100	$ 100	$ 100	$ 100	$ 100	$ 100	$ 100	$ 100
Anchor Guide	$ 175	$ 175	$ 175	$ 175	$ 175	$ 175	$ 175	$ 175	$ 175	$ 175	$ 175	$ 175	$ 175	$ 175
Contura radiation balloon therapy	$ 2,700	$ 2,700	$ 2,700	$ 2,633	$ 2,500	$ 2,634	$ 1,750	$ 2,379	$ 2,013	$ 2,314	$ 2,627	$ 2,692	$ 2,412	$ 2,616
OED			$ -	$ -	$ -	$ -	$ -	$ -	$ -	$ -	$ -	$ -	$ -	$ 500
Gamma Detection	$ 18,875	$ 18,875	$ 18,494	$ 18,000	$ 18,000	$ 18,000	$ 18,000	$ 18,000	$ 18,000	$ 18,000	$ 18,000	$ 18,000	$ 18,000	$ 18,000
Revenue ($ in millions)														
Encor Biopsy Equipment				$ 1.1	$ 0.5	$ 0.6	$ 1.0	$ 1.2	$ 3.3	$ 0.9	$ 0.9	$ 0.8	$ 0.8	$ 3.4	$ 2.8
Sencosr Biopsy Equipment				$ 0.1	$ 0.0	$ 0.0	$ 0.0	$ 0.0	$ 0.1	$ 0.0	$ 0.0	$ 0.0	$ 0.0	$ 0.1	$ 0.1
Encor Biopsy	$ 1.1	$ 5.6	$ 10.3	$ 3.3	$ 3.8	$ 3.8	$ 4.4	$ 15.3	$ 4.7	$ 5.4	$ 5.3	$ 6.2	$ 21.5	$ 27.9
Sencosr Biopsy	$ 0.6	$ 0.6	$ 0.7	$ 0.2	$ 0.2	$ 0.2	$ 0.2	$ 0.8	$ 0.2	$ 0.2	$ 0.2	$ 0.2	$ 0.9	$ 1.0
Biopsy Products	$ 1.7	$ 6.2	$ 11.0	$ 3.5	$ 4.0	$ 3.9	$ 4.6	$ 16.1	$ 4.9	$ 5.6	$ 5.5	$ 6.4	$ 22.4	$ 28.9
Captive Markers	$ 1.4	$ 1.9	$ 2.5	$ 1.0	$ 1.0	$ 1.2	$ 1.4	$ 4.5	$ 1.4	$ 1.4	$ 1.6	$ 1.8	$ 6.2	$ 8.0
Non-captive Markers	$ 8.5	$ 8.5	$ 8.8	$ 2.3	$ 2.2	$ 2.2	$ 2.3	$ 9.0	$ 2.4	$ 2.3	$ 2.3	$ 2.4	$ 9.3	$ 9.5
Marker Products	$ 9.9	$ 10.4	$ 11.6	$ 3.3	$ 3.2	$ 3.4	$ 3.7	$ 13.6	$ 3.8	$ 3.7	$ 3.9	$ 4.2	$ 15.5	$ 17.5
Biopsy Equipment	$ 0.6	$ 1.4	$ 1.2	$ 0.5	$ 0.6	$ 1.0	$ 1.2	$ 3.3	$ 0.9	$ 0.9	$ 0.9	$ 0.9	$ 3.5	$ 2.9
Single Step	$ -	$ -	$ -	$ -	$ -	$ -	$ -	$ -	$ -	$ -	$ 0.1	$ 0.1	$ 0.2	$ 1.0
Shape Select	$ -	$ -	$ -	$ -	$ -	$ -	$ -	$ -	$ -	$ -	$ 0.0	$ 0.1	$ 0.1	$ 0.3
Anchor Guide	$ 0.2	$ 0.2	$ 0.1	$ 0.0	$ 0.0	$ 0.0	$ 0.0	$ 0.1	$ -	$ -	$ -	$ -	$ -	$ -
Excision/Therapy	$ 0.2	$ 0.2	$ 0.1	$ 0.0	$ 0.0	$ 0.0	$ 0.0	$ 0.1	$ -	$ -	$ 0.1	$ 0.1	$ 0.2	$ 1.3
Contura radiation balloon therapy	$ -	$ -	$ -	$ -	$ -	$ 0.0	$ 0.2	$ 0.3	$ 0.6	$ 0.7	$ 1.1	$ 1.7	$ 2.5	$ 6.0	$ 14.0
OED	$ -	$ -	$ -	$ -	$ -	$ -	$ -	$ -	$ -	$ -	$ -	$ -	$ -	$ -	$ 0.3
Gamma Detection	$ 1.4	$ 1.1	$ 1.4	$ 0.4	$ 0.2	$ 0.4	$ 0.4	$ 1.4	$ 0.5	$ 0.5	$ 0.5	$ 0.5	$ 2.0	$ 2.3
Total Revenue	$ 13.8	$ 19.3	$ 25.5	$ 7.7	$ 8.1	$ 8.9	$ 10.3	$ 35.0	$ 10.7	$ 11.7	$ 12.5	$ 14.6	$ 49.5	$ 67.2
REVENUE ANALYSIS - (% of Total Revenue)														
Biopsy Products	12.4%	32.0%	43.1%	45.5%	49.5%	44.3%	44.9%	46.0%	45.7%	47.9%	43.7%	44.1%	45.2%	43.0%
Marker Products	71.9%	54.0%	45.5%	42.7%	39.8%	37.7%	35.6%	38.7%	35.2%	31.6%	30.8%	28.5%	31.3%	26.0%
Biopsy Equipment	4.2%	7.2%	4.8%	6.5%	7.6%	11.6%	11.6%	9.5%	8.2%	7.5%	6.8%	5.9%	7.0%	4.3%
Excision/Therapy	1.4%	1.2%	0.5%	0.5%	0.3%	0.4%	0.3%	0.4%	0.0%	0.0%	0.8%	0.7%	0.4%	1.9%
Contura radiation balloon therapy	0.0%	0.0%	0.0%	0.0%	0.3%	2.1%	3.3%	1.6%	6.4%	9.0%	13.9%	17.3%	12.1%	20.9%
Gamma Detection	9.9%	5.5%	6.1%	4.9%	2.4%	4.0%	4.2%	3.9%	4.5%	4.1%	4.0%	3.6%	4.0%	3.5%
	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	99.6%
REVENUE Growth - (Year-over-Year)														
Biopsy Products	n/a	257.1%	78.4%	52.3%	52.3%	39.8%	43.1%	46.4%	39.6%	39.7%	38.7%	38.6%	39.1%	29.1%
Marker Products	n/a	5.2%	11.8%	19.3%	11.7%	18.8%	16.5%	16.5%	14.3%	14.5%	15.0%	13.0%	14.2%	12.9%
Biopsy Equipment	n/a	139.6%	-12.1%	61.8%	55.9%	241.9%	461.4%	174.1%	76.0%	41.1%	-17.1%	-28.6%	3.5%	-16.0%
Excision/Therapy	n/a	19.0%	-42.3%	0.0%	-20.0%	33.3%	-20.0%	-4.5%	-100.0%	-100.0%	n/a	827.7%	637.5%	983.2%	134.0%
Contura radiation balloon therapy	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Gamma Detection	n/a	-22.0%	46.6%	-13.1%	-44.6%	-8.9%	13.0%	-12.7%	28.6%	149.4%	43.2%	20.8%	47.3%	17.0%
Total Revenue	n/a	40.0%	32.7%	32.0%	28.6%	40.0%	46.5%	37.2%	39.0%	44.5%	40.7%	41.3%	41.4%	35.8%

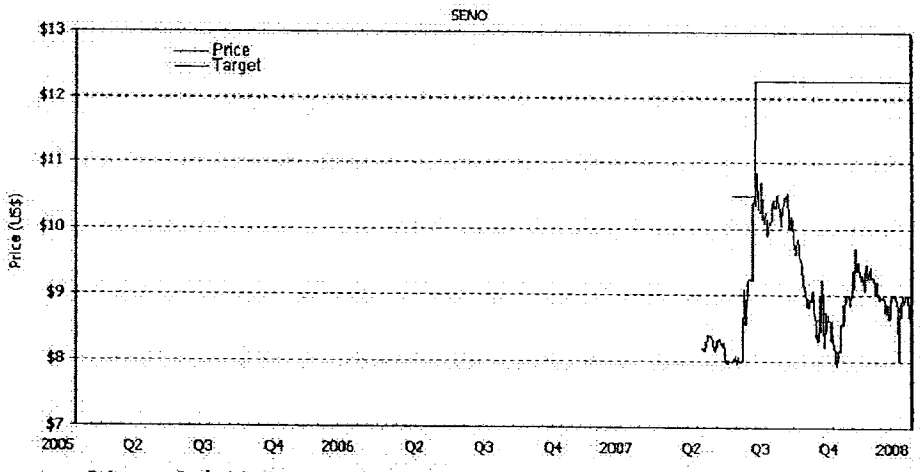
Source: Company reports and Canaccord Adams estimates

APPENDIX: IMPORTANT DISCLOSURES

Analyst Certification: Each authoring analyst of Canaccord Adams whose name appears on the front page of this investment research hereby certifies that (i) the recommendations and opinions expressed in this investment research accurately reflect the authoring analyst's personal, independent and objective views about any and all of the designated investments or relevant issuers discussed herein that are within such authoring analyst's coverage universe and (ii) no part of the authoring analyst's compensation was, is, or will be, directly or indirectly, related to the specific recommendations or views expressed by the authoring analyst in the investment research.

Site Visit: An analyst has visited the issuer's material operations in Aliso Viejo, California. No payment or reimbursement was received from the issuer for the related travel costs.

Price Chart:*



	Date	Analyst	Rating	Target Price
1)	05/08/07	JM	Buy	10.50
2)	06/07/07	JM	Buy	12.25

* Price charts assume event 1 indicates initiation of coverage or the beginning of the measurement period.

Distribution of Ratings:
Global Stock Ratings
(as of 1 February 2008)

Rating	Coverage Universe #	Coverage Universe %	IB Clients %
Buy	313	60.3%	43.1%
Speculative Buy	62	11.9%	71.0%
Hold	128	24.7%	24.2%
Sell	16	3.1%	6.3%
	519	100.0%	

Canaccord Ratings System:
BUY: The stock is expected to generate risk-adjusted returns of over 10% during the next 12 months.
HOLD: The stock is expected to generate risk-adjusted returns of 0-10% during the next 12 months.
SELL: The stock is expected to generate negative risk-adjusted returns during the next 12 months.
NOT RATED: Canaccord Adams does not provide research coverage of the relevant issuer.

"Risk-adjusted return" refers to the expected return in relation to the amount of risk associated with the designated investment or the relevant issuer.

Risk Qualifier: SPECULATIVE: Stocks bear significantly higher risk that typically cannot be valued by normal fundamental criteria. Investments in the stock may result in material loss.

Canaccord Adams Research Disclosures as of 20 February 2008

Company	Disclosure
SenoRx	1A, 2, 3, 5, 7

1	The relevant issuer currently is, or in the past 12 months was, a client of Canaccord Adams or its affiliated companies. During this period, Canaccord Adams or its affiliated companies provided the following services to the relevant issuer: A. investment banking services. B. non-investment banking securities-related services. C. non-securities related services.
2	In the past 12 months, Canaccord Adams or its affiliated companies have received compensation for Corporate Finance/Investment Banking services from the relevant issuer.
3	In the past 12 months, Canaccord Adams or any of its affiliated companies have been lead manager, co-lead manager or co-manager of a public offering of securities of the relevant issuer or any publicly disclosed offer of securities of the relevant issuer or in any related derivatives.
4	Canaccord Adams acts as corporate broker for the relevant issuer and/or Canaccord Adams or any of its affiliated companies may have an agreement with the relevant issuer relating to the provision of Corporate Finance/Investment Banking services.
5	Canaccord Adams or any of its affiliated companies is a market maker or liquidity provider in the securities of the relevant issuer or in any related derivatives.
6	In the past 12 months, Canaccord Adams, its partners, affiliated companies, officers or directors, or any authoring analyst involved in the preparation of this investment research has provided services to the relevant issuer for remuneration, other than normal course investment advisory or trade execution services.
7	Canaccord Adams intends to seek or expects to receive compensation for Corporate Finance/Investment Banking services from the relevant issuer in the next six months.
8	The authoring analyst, a member of the authoring analyst's household, or any individual directly involved in the preparation of this investment research, has a long position in the shares or derivatives, or has any other financial interest in the relevant issuer, the value of which increases as the value of the underlying equity increases.
9	The authoring analyst, a member of the authoring analyst's household, or any individual directly involved in the preparation of this investment research, has a short position in the shares or derivatives, or has any other financial interest in the relevant issuer, the value of which increases as the value of the underlying equity decreases.
10	Those persons identified as the author(s) of this investment research, or any individual involved in the preparation of this investment research, have purchased/received shares in the relevant issuer prior to a public offering of those shares, and such person's name and details are disclosed above.
11	A partner, director, officer, employee or agent of Canaccord Adams and its affiliated companies, or a member of his/her household, is an officer, or director, or serves as an advisor or board member of the relevant issuer and/or one of its subsidiaries, and such person's name is disclosed above.
12	As of the month end immediately preceding the date of publication of this investment research, or the prior month end if publication is within 10 days following a month end, Canaccord Adams or its affiliate companies, in the aggregate, beneficially owned 1% or more of any class of the total issued share capital or other common equity securities of the relevant issuer or held any other financial interests in the relevant issuer which are significant in relation to the investment research (as disclosed above).
13	As of the month end immediately preceding the date of publication of this investment research, or the prior month end if publication is within 10 days following a month end, the relevant issuer owned 1% or more of any class of the total issued share capital in Canaccord Adams or any of its affiliated companies.
14	Other specific disclosures as described above.

Canaccord Adams is the business name used by certain subsidiaries of Canaccord Capital Inc., including Canaccord Adams Inc., Canaccord Adams Limited, and Canaccord Adams, a division of Canaccord Capital Corporation. Clients of Canaccord Adams, in the past 12 months, may have been clients of Canaccord Capital Corporation, Canaccord Capital (Europe) Limited, Canaccord Capital Corporation USA Inc., and/or Adams Harkness Financial Group Ltd.

The authoring analysts who are responsible for the preparation of this investment research are employed by Canaccord Adams, a securities broker-dealer with principal offices located in Vancouver, Calgary, Toronto, Montreal (all Canada), Boston, New York, San Francisco (all US) and London (UK).

In the event that this is compendium investment research (covering six or more relevant issuers), Canaccord Adams and its affiliated companies may choose to provide specific disclosures of the subject companies by reference, as well as its policies and procedures regarding the dissemination of investment research. To access this material or for more information, please send a request to Canaccord Adams Research, Attn: Disclosures, P.O. Box 10337 Pacific Centre, 2200-609 Granville Street, Vancouver, BC, Canada V7Y 1H2 or disclosures@canaccordadams.com.

The authoring analysts who are responsible for the preparation of this investment research have received (or will receive) compensation based upon (among other factors) the Corporate Finance/Investment Banking

revenues and general profits of Canaccord Adams. However, such authoring analysts have not received, and will not receive, compensation that is directly based upon or linked to one or more specific Corporate Finance/Investment Banking activities, or to recommendations contained in the investment research.

Canaccord Adams and its affiliated companies may have a Corporate Finance/Investment Banking or other relationship with the company that is the subject of this investment research and may trade in any of the designated investments mentioned herein either for their own account or the accounts of their customers, in good faith or in the normal course of market making. Accordingly, Canaccord Adams or their affiliated companies, principals or employees (other than the authoring analyst(s) who prepared this investment research) may at any time have a long or short position in any such designated investments, Related designated investments or in options, futures or other derivative instruments based thereon.

Some regulators require that a firm must establish, implement and make available a policy for managing conflicts of interest arising as a result of publication or distribution of investment research. This investment research has been prepared in accordance with Canaccord Adams' policy on managing conflicts of interest, and information barriers or firewalls have been used where appropriate. Canaccord Adams' policy is available upon request.

The information contained in this investment research has been compiled by Canaccord Adams from sources believed to be reliable, but (with the exception of the information about Canaccord Adams) no representation or warranty, express or implied, is made by Canaccord Adams, its affiliated companies or any other person as to its fairness, accuracy, completeness or correctness. Canaccord Adams has not independently verified the facts, assumptions, and estimates contained herein. All estimates, opinions and other information contained in this investment research constitute Canaccord Adams' judgement as of the date of this investment research, are subject to change without notice and are provided in good faith but without legal responsibility or liability.

Canaccord Adams salespeople, traders, and other professionals may provide oral or written market commentary or trading strategies to our clients and our proprietary trading desk that reflect opinions that are contrary to the opinions expressed in this investment research. Canaccord Adams' affiliates, proprietary trading desk, and investing businesses may make investment decisions that are inconsistent with the recommendations or views expressed in this investment research.

This investment research is provided for information purposes only and does not constitute an offer or solicitation to buy or sell any designated investments discussed herein in any jurisdiction where such offer or solicitation would be prohibited. As a result, the designated investments discussed in this investment research may not be eligible for sale in some jurisdictions. This investment research is not, and under no circumstances should be construed as, a solicitation to act as a securities broker or dealer in any jurisdiction by any person or company that is not legally permitted to carry on the business of a securities broker or dealer in that jurisdiction. This material is prepared for general circulation to clients and does not have regard to the investment objectives, financial situation or particular needs of any particular person. Investors should obtain advice based on their own individual circumstances before making an investment decision. To the fullest extent permitted by law, none of Canaccord Adams, its affiliated companies or any other person accepts any liability whatsoever for any direct or consequential loss arising from or relating to any use of the information contained in this investment research.

For Canadian Residents: This Investment Research has been approved by Canaccord Adams, a division of Canaccord Capital Corporation, which accepts responsibility for this Investment Research and its dissemination in Canada. Canadian clients wishing to effect transactions in any Designated Investment discussed should do so through a qualified salesperson of Canaccord Adams, a division of Canaccord Capital Corporation in their particular jurisdiction.

For United Kingdom Residents: This Investment Research complies with of the Financial Services Authority's Handbook's chapter on Conduct of Business and is approved by Canaccord Adams Limited, which is regulated and authorized by the Financial Services Authority, in connection with its distribution in the United Kingdom. This material is not for distribution in the United Kingdom to private customers, as defined under the rules of the Financial Services Authority. Canaccord Adams Limited accepts responsibility for this Investment Research and its dissemination in the United Kingdom. The information contained in this Investment Research is only intended for distribution in the UK to persons who qualify as intermediate customers or market counterparties, as defined under the rules of the Financial Services Authority.

For United States Residents: Canaccord Adams Inc., a US registered broker-dealer, accepts responsibility for this Investment Research and its dissemination in the United States. This Investment Research is intended for distribution in the United States only to certain US institutional investors. US clients wishing to effect transactions in any Designated Investment discussed should do so through a qualified salesperson of Canaccord Adams Inc.

For European Residents: If this Investment Research is intended for disclosure in any jurisdiction other than the United Kingdom, the US or Canada, then the relevant rules and regulatory requirements of that jurisdiction will apply.

Additional information is available on request.

ocument

citi

Company Focus

19 February 2008 | 18 pages

SenoRx Inc (SENO)

Estimate change ☑
Results ☑

4Q07 Earnings; Top-Line Strength Offset by Temporary GM Hiccup

- **SENO reported 4Q07 operating EPS of ($0.16), $0.07 below our expectations.** Higher total revs of $10.3M (+$0.6M vs. our est.) were more than offset by higher discretionary spending (+$1.1M) and a lower gross margin (-510 bp). GAAP EPS was ($0.23) and included a $1.3 million non-cash charge (or EPS of $0.07) related to the retirement of subordinated debt.

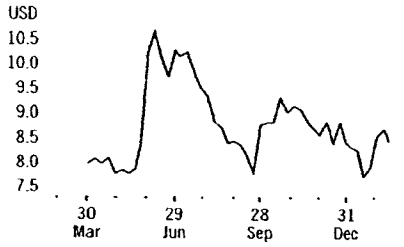
- **The quarter was respectable as total revs exceed expectations and gross margin weakness should reverse in 2008** – Total revs of $10.3M (+43% Y/Y) included biopsy revs of $5.9M (+$0.5M vs. our est.), marker revs of $3.5M (+$0.2M), gamma detection revs of $0.5M (in-line), and brachytherapy revs of $0.3M (-$0.1M). GM was negatively impacted by: (1) service enhancements (-130 bp Q/Q), (2) Int'l mix with 12 systems sold overseas (-130 bp Q/Q), and (3) revaluation of inventory as certain products shift mftg location (-150 bp Q/Q).

- **EnCor breast biopsy a key driver once again** – Biopsy capital equipment sales accounted for revs of $1.2M (+$0.3M vs. our est.) as a higher percentage of customers purchased biopsy systems outright rather than through purchase-sale agreements (PSA). Biopsy disposable revs were $4.7M (+$0.2M) and should benefit in 2008 from the 80 systems placed in 4Q. About 120 Contura units were sold in 4Q (ASP $2,750) with continued adoption expected in 2008.

- **Mgmt reiterated 2008 revenue guidance to $46-50M (we are at $49M)** – We maintain our Hold rating and $12 PT which is based on an equal-weighted average of a P/S of 3.5x our 2009E revs of $67M and DCF valuation of $11.

Hold/Speculative	**2S**
Price (15 Feb 08)	US$8.61
Target price	US$12.00
Expected share price return	39.4%
Expected dividend yield	0.0%
Expected total return	**39.4%**
Market Cap	US$148M

Price Performance (RIC: SENO.O, BB: SENO US)



EPS	Q1	Q2	Q3	Q4	FY	FC Cons
2007A	-0.20A	-0.15A	-0.10A	-0.16A	-0.59A	-0.53A
2008E	**-0.10E**	**-0.08E**	**-0.08E**	**-0.02E**	**-0.28E**	**-0.20E**
Previous	-0.07E	-0.04E	-0.05E	0.00E	-0.16E	na
2009E	na	na	na	na	**0.02E**	**0.16E**
Previous	na	na	na	na	0.09E	na
2010E	na	na	na	na	**0.22E**	**0.57E**
Previous	na	na	na	na	0.20E	na

Source: Powered by dataCentral. FC Cons: First Call Consensus.

Amit Bhalla
+1-212-816-4069
amit1.bhalla@citi.com

See Appendix A-1 for Analyst Certification and important disclosures.

Fiscal year end 31-Dec	2006	2007	2008E	2009E	2010E
Valuation Ratios					
P/E adjusted (x)	-5.3	-14.6	nm	nm	39.3
EV/EBITDA adjusted (x)	nm	nm	nm	147.8	22.2
P/BV (x)	-1.3	-6.0	-6.6	-8.1	-13.4
Dividend yield (%)	0.0	0.0	0.0	0.0	0.0
Per Share Data (US$)					
EPS adjusted	-1.63	-0.59	-0.28	0.02	0.22
EPS reported	-1.63	-0.68	-0.28	0.02	0.22
BVPS	-6.40	-1.43	-1.31	-1.06	-0.64
DPS	0.00	0.00	0.00	0.00	0.00
Profit & Loss (US$M)					
Net sales	26	35	49	67	80
Operating expenses	-36	-45	-54	-67	-74
EBIT	**-10**	**-10**	**-5**	**0**	**6**
Net interest expense	-1	1	1	1	1
Non-operating/exceptionals	-4	-1	0	0	0
Pre-tax profit	**-15**	**-10**	**-5**	**1**	**7**
Tax	0	0	0	0	-3
Extraord./Min.Int./Pref.div.	0	0	0	0	0
Reported net income	**-15**	**-10**	**-5**	**0**	**4**
Adjusted earnings	-15	-9	-5	0	4
Adjusted EBITDA	-9	-9	-4	1	7
Growth Rates (%)					
Sales	32.5	37.3	38.5	38.0	20.1
EBIT adjusted	-29.9	7.3	44.2	98.9	nm
EBITDA adjusted	-32.6	9.1	50.2	125.8	547.2
EPS adjusted	-73.7	63.9	52.7	106.6	nm
Cash Flow (US$M)					
Operating cash flow	**-9**	**-5**	**-1**	**3**	**8**
Depreciation/amortization	1	1	1	1	1
Net working capital	0	1	-1	-1	0
Investing cash flow	**-1**	**-1**	**-1**	**-1**	**-1**
Capital expenditure	-1	-1	-1	-1	-1
Acquisitions/disposals	0	0	0	0	0
Financing cash flow	**17**	**47**	**0**	**0**	**0**
Borrowings	17	0	0	0	0
Dividends paid	0	0	0	0	0
Change in cash	**7**	**41**	**-2**	**2**	**7**
Balance Sheet (US$M)					
Total assets	**20**	**59**	**59**	**64**	**73**
Cash & cash equivalent	7	48	46	48	55
Accounts receivable	4	5	7	9	11
Net fixed assets	1	1	1	1	1
Total liabilities	**34**	**34**	**35**	**37**	**39**
Accounts payable	4	3	4	4	5
Total Debt	14	14	14	14	14
Shareholders' funds	**-14**	**26**	**24**	**27**	**35**
Profitability/Solvency Ratios (%)					
EBITDA margin adjusted	-36.6	-24.3	-8.7	1.6	8.8
ROE adjusted	na	na	na	na	na
ROIC adjusted	-194.2	-174.0	-105.2	-4.4	50.1
Net debt to equity	na	-133.8	-133.6	-125.1	-119.3
Total debt to capital	nm	34.9	36.6	33.5	28.5

For further data queries on Citigroup's full coverage universe please contact CIR Data Services Americas at CIRDataServicesAmericas@citigroup.com or +1-212-816-5336

Powered by: dataCentral

Investment Conclusions

SENO reported 4Q07 operating EPS of ($0.16), $0.07 below our expectations and $0.08 below consensus. Higher-than-expected total revenues of $10.3 million (+$0.6 million vs. our est.) were more than offset by higher discretionary spending (+$1.1 million) and a lower gross margin (-510 bp) leading to the variance from our estimates. GAAP EPS was ($0.23) and included a $1.3 million non-cash charge related to the retirement of subordinated debt. We excluded this non-cash charge in our operating EPS calculation.

This was a respectable quarter for SenoRx, as total revenues exceeded our expectations and consensus. Total revenues of $10.3 million (+43%) included biopsy revenues of $5.9 million (+$0.5 million), marker revenues of $3.5 million (+$0.2 million), gamma detection and other revenues of $0.5 million (in line), and brachytherapy revenues of $0.3 million (-$0.1 million). The EnCor breast biopsy product was the key source of upside in the quarter as the company ended 2007 with 536 system placements (vs. our est. of 509). This is an important metric as system placements are viewed as a lead indicator for future revenues and the placement upside in the quarter is a positive. The company also continued expanding its sales force organization, which now consists of 66 employees (vs. 59 in 3Q07), as well as its physician training initiatives (64 training seminars with 1,355 new clinicians trained in 2007).

Breast biopsy (EnCor) capital equipment and disposables were the key drivers in the quarter. Within the biopsy segment, capital equipment accounted for revenues of $1.2 million (+$0.3 million) while disposables accounted for revenues of $4.7 million (+$0.2 million). Capital equipment sales were notably higher than our expectations as a higher percentage of customers purchased biopsy systems outright as opposed to acquiring them through purchase-sale agreements (PSA). We estimate that the installation mix during 4Q07 was 70% outright sales versus 30% PSA, and should probably be in the 60/40 range for 2008 For the brachytherapy segment (Contura), the company sold about 120 Contura units (assuming an average selling price of $2,750) and the product is being fully launched as of January 2008.

Gross margin was a disappointment in the quarter, but should rebound in 2008. Gross margin in the quarter was 55.9%, 510 bp below our estimate and down 410 bp compared to 3Q07. Management indicated that the sequential decline was attributed to three factors. (1) About 130 bp of the Q/Q decline was due to mix as the company conducted system enhancements in the MR arena to leverage gross margin gains on future disposable sales. (2) The quarter saw a greater number of International biopsy system purchases by distributors which are at lower ASPs (about 12 of the 80 placements were overseas and led to a 130 bp gross margin drop Q/Q). And (3) about 150 bp of the decline was due to a revaluation of inventory as certain products will be manufactured in Thailand in the future and some products (such as the anchor guide) were discontinued.

Management reiterated the 2008 financial guidance it provided on December 20. Revenues are expected to be $46-50 million (we are at $49 million) with deferred and equity-based compensation of $2.8-3.2 million (we are at $3.0 million). In addition, management expects patent litigation costs related to the HOLX balloon brachytherapy case to be $1.4-1.7 million for the year ahead.

We are maintaining our Hold rating and price target of $12. Our price target is based on an equally-weighted average of a 3.5x P/S multiple on our revised 2009 sales of $67 million (from $70 million) and our DCF valuation of $11.

Figure 1. SenoRx Biopsy Console Placements and Disposable Units Sold ($ in millions except ASP's)

	BIOPSY REVS ($MM)			CONSOLE PLACEMENTS & PRODUCTIVITY							MARKERS		
	Capital Equipment	Disposables	Total	EnCor Placed in Qtr	PSA Placed in Qtr	Total Installed Base	Qtrly Units Placed	Disposable Units Sold	Q/Q New Disposable Units Sold	Units per Console	Market Unit Placements	ASPs	Marker Revenues
1Q05A	$0.5	$1.1	$1.6	22	10	78		6,397		82.0	36,259	$72.7	$2.6
2Q05A	$0.2	$1.5	$1.7	22	6	106	28	8,503	2,106	80.2	34,905	$74.1	$2.6
3Q05A	$0.5	$1.6	$2.0	22	2	130	24	9,153	650	70.4	34,743	$72.5	$2.5
4Q05A	$0.3	$2.0	$2.3	22	12	164	34	12,081	2,928	73.7	36,820	$72.4	$2.7
1Q06A	$0.3	$2.3	$2.7	16	18	198	34	12,287	206	62.1	37,972	$73.0	$2.8
2Q06A	$0.4	$2.6	$3.0	19	17	234	36	14,880	2,593	63.6	36,999	$78.3	$2.9
3Q06A	$0.4	$2.7	$3.1	15	23	272	38	16,933	2,053	62.3	37,870	$72.2	$2.7
4Q06A	$0.3	$3.3	$3.6	23	22	317	45	21,746	4,813	68.6	39,397	$82.1	$3.2
1Q07A	$0.5	$3.5	$4.0	22	21	360	43	16,760	-4,986	46.6	44,000	$75.0	$3.3
2Q07A	$0.6	$4.0	$4.6	23	23	406	46	19,150	2,391	47.2	44,000	$75.0	$3.3
3Q07A	$1.0	$3.9	$5.0	35	15	456	50	18,790	-360	41.2	46,768	$73.0	$3.4
4Q07A	$1.2	$4.7	$5.9	55	25	536	80	22,517	3,727	42.0	48,612	$73.0	$3.5
1Q08E	$0.8	$4.9	$5.7	30	20	586	50	23,367	850	39.9	53,240	$70.0	$3.7
2Q08E	$0.8	$5.2	$6.0	33	22	641	55	24,617	1,250	38.4	53,240	$69.5	$3.7
3Q08E	$1.0	$5.1	$6.1	39	26	706	65	24,317	-300	34.4	56,589	$69.0	$3.9
4Q08E	$1.1	$5.6	$6.7	42	28	776	70	26,817	2,500	34.6	58,820	$68.4	$4.0
2005A	$1.4	$6.1	$7.6	88	30	164		36,134		220.3	142,727	$72.9	$10.4
2006A	$1.4	$11.0	$12.4	73	80	317	153	65,846	29,712	207.7	152,239	$76.4	$11.6
2007A	$3.3	$16.2	$19.5	135	84	536	219	77,218	11,372	144.1	183,380	$74.0	$13.6
2008E	$3.6	$20.8	$24.4	144	96	776	240	99,119	21,901	127.7	221,889	$69.2	$15.4

Source: Company Reports and CIR Estimates

Figure 2. SENO – 4Q07 Variance Analysis – Income Statement ($ in millions except EPS)

	Estimate		Actual		
	Amount	Y/Y %Chg	Amount	Y/Y %Chg	Variance
Biopsy					
- Capital equipment	0.9	238%	1.2	353%	0.3
- Disposables	4.6	37%	4.7	43%	0.2
Total biopsy (EnCor)	5.4	52%	5.9	65%	0.5
Markers	3.4	5%	3.5	10%	0.2
Gamma Detection and Other	0.5	43%	0.5	43%	0.0
Brachytherapy (Contura)	0.4	NA	0.3	NA	(0.1)
Excision products	0.0	-31%	0.0	-31%	0.0
Net sales	**9.8**	**35%**	**10.3**	**43%**	**0.6**
COGS	3.8	-7%	4.5	12%	(0.7)
COGS x-SBC	3.7	NM	4.5	NM	(0.8)
(SBC w/in COGS)	0.1	NM	0.1	NM	0.1
Gross Profit	**6.0**	**90%**	**5.8**	**84%**	**(0.2)**
Sales & marketing	4.6	5%	5.9	36%	(1.4)
Sales & marketing x-SBC	4.2	NM	5.6	NM	(1.4)
(SBC w/in Sales & marketing)	0.3	NM	0.3	NM	0.0
R&D	1.8	124%	1.7	114%	0.1
R&D x-SBC	1.6	NM	1.5	NM	0.1
(SBC w/in R&D)	0.2	NM	0.2	NM	0.1
G&A	1.2	214%	1.1	200%	0.1
R&D x-SBC	1.0	NM	1.0	NM	(0.0)
(SBC w/in R&D)	0.1	NM	0.1	NM	0.1
Total Op. Expense	7.6	19%	8.7	37%	(1.1)
Operating Income	**(1.6)**	**NM**	**(2.9)**	**NM**	**(1.3)**
Total Non-Op Income	0.0	NM	0.2	NM	0.2
Pre-tax Income	**(1.6)**	**NM**	**(2.7)**	**NM**	**(1.1)**
Taxes	0.0	NM	0.0	NM	0.0
Tax rate	0.0%	NM	0.0%	NM	NM
Net Income	**(1.6)**	**NM**	**(2.7)**	**NM**	**(1.1)**
Shares (MM)	17.3	NM	17.2	NM	(0.1)
Operating EPS (incl. FAS 123R)	**($0.09)**	**NM**	**($0.16)**	**NM**	**($0.07)**
GAAP EPS	**($0.17)**	**NM**	**($0.23)**	**NM**	**($0.06)**
Margin Analysis					
Sales	100.0%		100.0%		
COGS	39.0%		44.1%		-5.1%
Gross profit	61.0%		55.9%		-5.1%
Sales & marketing	47.0%		57.6%		-10.6%
R&D	18.5%		16.1%		2.4%
G&A	12.0%		10.6%		1.4%
Operating income	-16.5%		-28.4%		-11.9%
Non-operating items	-0.1%		1.8%		1.9%
Pre-Tax Income	-16.5%		-26.5%		-10.0%
Net Income	-16.5%		-26.5%		-10.0%

NM = Not Meaningful; *GAAP EPS includes one time items
Source: Company Reports and CIR Estimates

Figure 3. Business Segment Highlights (sales figures in millions)

BIOPSY DISPOSABLE PRODUCTS

	4Q07	3Q07	4Q06
Actual	$4.7	$3.9	$3.3
CIR Estimate	$4.6		

YoY Growth	
Actual	43%

- Disposables grew roughly 4% Y/Y and 20% Q/Q to about 22,500
- ASP remained essentially unchanged for biopsy disposables

BIOPSY CAPITAL EQUIPMENT PRODUCTS

	4Q07	3Q07	4Q06
Actual	$1.2	$1.0	$0.3
CIR Estimate	$0.9		

YoY Growth	
Actual	353%

- Total EnCor installed base of 536 at the end of 3Q07 (+80 units during the quarter)
- EnCor units sold outright were higher than those placed through purchase-sale agreements (PSA's); we estimate a 70/30% split
- About 12 of the 80 unit placements were overseas at lower ASPs

DIAGNOSTIC ADJUNCT PRODUCTS

	4Q07	3Q07	4Q06
Actual	$4.1	$3.7	$3.6
CIR Estimate	$3.9		

YoY Growth	
Actual	14%

- Tissue markers were the key driver in this segment with no major changes in ASPs (we estimate ASP about $73 per marker)

THERAPEUTIC DISPOSABLES (BALLOON BRACHYTHERAPY)

	4Q07	3Q07	4Q06
Actual	$0.3	$0.2	$0.0
CIR Estimate	$0.4		

YoY Growth	
Actual	NA

- About 120 Contura units sold in 3Q07 (based on an ASP of $2,750vs. 68 in 3Q07
- Contura was evaluated at 34 clinical sites by the end of 2007 (exceeding mgmt's 20 site target)
- 3 training symposium held for Contura in 4Q07

SALES FORCE & PHYSICIAN TRAINING

- 66 total employees at end of 3Q07 (vs. 59 in 3Q07)
- This included 41 direct reps, 20 clinical specialists and 5 brachytherapy specialists
- 64 training seminars hosted and 1,355 new physicians trained in 2007

Source: Company Reports and CIR Estimates

Management Guidance & Key Changes to Our Model

For 2008, management reiterated the financial guidance it provided on December 20. Revenues are expected to be $46-50 million (we are at ~$49 million) with deferred and equity-based compensation of $2.8-3.2 million (we are at $3.0 million). In addition, management expects patent litigation costs related to the HOLX balloon brachytherapy case to be $1.4-1.7 million for the year ahead.

We are decreasing our EPS to ($0.28) from ($0.16) in 2008 and to $0.02 from $0.09 in 2009. For 2008, we are decreasing our revenues by $2 million to $48.5 million (based mainly on more conservative Contura and Biopsy revenues) and reducing gross margin by 30 bp. For 2009, we are decreasing

our revenues by $3.5 million to $66.9 million (based mainly on more conservative Contura and Biopsy revenues).

Figure 4. Key Changes to Our Model

	2008E		2009E	
	Current	**Previous**	**Current**	**Previous**
Biopsy	$24.4M	$25.7M	$29.1M	$31.6M
Markers	$15.4M	$15.1M	$17.6M	$17.2M
Gamma Detection and Other	$2.7M	$2.0M	$2.8M	$2.3M
Brachytherapy	$5.4M	$7.2M	$15.0M	$17.2M
Excision Products	$0.6M	$0.5M	$2.4M	$2.0M
Total Revenues	**$48.5M**	**$50.5M**	**$66.9M**	**$70.4M**
COGS	$17.7M	$18.3M	$21.5M	$23.6M
SG&A	$29.1M	$28.0M	$36.8M	$36.6M
R&D	$7.1M	$7.5M	$8.7M	$8.1M
Operating EPS	**($0.28)**	**($0.16)**	**$0.02**	**$0.09**

NC = No Change from previous estimates

Source: Company Reports and CIR Estimates

Figure 5. SenoRx – Annual Income Statement ($ in millions, except per share)

Fiscal Year End: December	2004A	2005A	2006A	2007A	2008E	2009E	2010E	2011E
TOTAL Net Sales	**13.8**	**19.3**	**25.5**	**35.0**	**48.5**	**66.9**	**80.4**	**94.7**
COGS	6.4	10.1	13.5	15.1	17.7	21.5	24.2	27.6
COGS (x-SBC)	6.4	10.1	13.5	14.9	17.4	21.2	23.9	27.3
(SBC w/in COGS)	0.0	0.0	0.1	0.2	0.3	0.3	0.3	0.3
Gross Profit	**7.3**	**9.1**	**12.0**	**19.9**	**30.8**	**45.5**	**56.1**	**67.1**
Sales & Marketing	7.5	10.1	15.0	19.0	23.3	29.4	33.0	37.9
Sales & Marketing (x-SBC)	7.3	9.7	14.6	18.4	22.5	28.6	32.2	37.1
(SBC w/in Sales & Marketing)	0.2	0.4	0.4	0.6	0.8	0.8	0.8	0.8
Research & Development	4.8	4.9	5.3	6.4	7.1	8.7	9.2	10.4
R&D (x-SBC)	4.6	4.6	4.9	5.8	6.5	8.1	8.6	9.8
(SBC w/in R&D)	0.2	0.3	0.4	0.6	0.6	0.6	0.6	0.6
General & Administrative	1.7	2.1	2.1	4.2	5.8	7.4	8.0	7.6
G&A (x-SBC)	1.3	1.6	1.8	3.4	4.4	6.0	6.6	6.2
(SBC w/in G&A)	0.4	0.6	0.2	0.8	1.4	1.4	1.4	1.4
Total Op. Expense	14.0	17.2	22.4	29.6	36.2	45.5	50.2	55.9
Operating Income	**(6.7)**	**(8.0)**	**(10.4)**	**(9.7)**	**(5.4)**	**(0.1)**	**5.9**	**11.2**
Total Non-Op expense (income)	0.1	0.6	5.0	(1.0)	(0.5)	(0.6)	(0.8)	(1.0)
Pre-tax Income	**(6.8)**	**(8.6)**	**(15.4)**	**(8.7)**	**(4.9)**	**0.5**	**6.7**	**12.2**
Tax Rate	-0.1%	-0.1%	0.0%	0.0%	0.0%	38.0%	38.0%	38.0%
Income Taxes	0.0	0.0	0.0	0.0	0.0	0.2	2.6	4.6
Net Income	**(6.8)**	**(8.6)**	**(15.4)**	**(8.7)**	**(4.9)**	**0.3**	**4.2**	**7.6**
Avg. Shares	5.3	9.2	9.4	14.7	17.5	18.3	19.0	19.7
Operating EPS	**($1.30)**	**($0.94)**	**($1.63)**	**($0.59)**	**($0.28)**	**$0.02**	**$0.22**	**$0.38**
GAAP Net Income	(6.8)	(8.6)	(15.4)	(9.9)	(4.9)	0.3	4.2	7.6
GAAP EPS	**($1.30)**	**($0.94)**	**($1.63)**	**($0.68)**	**($0.28)**	**$0.02**	**$0.22**	**$0.38**

* Operating EPS excludes non-recurring one time items (FAS 123R adjustments made for 2006 and future periods)

A = Actual; E = Citi Investment Research estimates

Source: Company Reports and CIR Estimates

Figure 6. SenoRx – Annual Margin and Growth Analysis

MARGIN ANALYSIS	2004A	2005A	2006A	2007A	2008E	2009E	2010E	2011E
Total Net Sales	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%
COGS	46.7%	52.5%	52.9%	43.2%	36.5%	32.1%	30.1%	29.2%
Gross Profit (x-SBC)	53.5%	47.7%	47.3%	57.4%	64.1%	68.4%	70.2%	71.2%
Gross Profit	53.3%	47.5%	47.1%	56.8%	63.5%	67.9%	69.9%	70.8%
Sales & Marketing	54.6%	52.7%	59.0%	54.3%	48.0%	44.0%	41.0%	40.0%
Sales & Marketing (x-SBC)	53.3%	50.4%	57.4%	52.7%	46.4%	42.8%	40.0%	39.2%
R&D	34.8%	25.5%	20.9%	18.1%	14.6%	13.0%	11.5%	11.0%
R&D (x-SBC)	33.5%	24.0%	19.3%	16.4%	13.4%	12.1%	10.8%	10.4%
G&A	12.4%	11.0%	8.0%	12.0%	12.0%	11.0%	10.0%	8.0%
G&A (x-SBC)	9.4%	8.1%	7.2%	9.8%	9.1%	8.9%	8.3%	6.5%
Total Op. Expense	101.9%	89.2%	87.9%	84.4%	74.6%	68.0%	62.5%	59.0%
Operating Income	-48.5%	-41.6%	-40.8%	-27.5%	-11.1%	-0.1%	7.4%	11.8%
Total Non-Op	1.1%	3.1%	19.6%	-2.8%	-1.0%	-0.9%	-1.0%	-1.1%
Pre-tax Income	-49.6%	-44.7%	-60.4%	-24.7%	-10.1%	0.8%	8.4%	12.9%
Income Taxes	0.0%	0.1%	0.0%	0.0%	0.0%	0.3%	3.2%	4.9%
Net Income	-49.6%	-44.8%	-60.5%	-24.7%	-10.1%	0.5%	5.2%	8.0%

YEAR/YEAR Growth	2004A	2005A	2006A	2007A	2008E	2009E	2010E	2011E
Total Net Sales	33.8%	40.0%	32.5%	37.3%	38.5%	38.0%	20.1%	17.9%
COGS	32.8%	57.5%	33.6%	12.0%	17.0%	21.4%	12.8%	14.0%
Gross Profit	34.7%	24.7%	31.2%	65.9%	54.8%	47.5%	23.5%	19.6%
Sales & Marketing	-5.9%	35.2%	48.2%	26.5%	22.5%	26.4%	11.9%	15.0%
R&D	97.2%	102.4%	108.6%	119.4%	111.8%	122.5%	106.2%	112.8%
G&A	142.8%	123.8%	97.0%	204.1%	138.5%	126.9%	109.2%	94.3%
Total Op. Expense	-0.7%	22.6%	30.6%	31.9%	22.4%	25.7%	10.4%	11.3%
Operating Income	-22.9%	20.2%	29.9%	NM	-44.2%	-98.9%	NM	89.8%
Total Non-Op	55.8%	301.4%	742.8%	-119.6%	-49.2%	20.0%	33.3%	25.0%
Pre-tax Income	-22.0%	26.3%	79.0%	NM	-43.7%	-111.1%	NM	82.0%
Income Taxes	NA	NA	NA	NA	NM	NM	NM	NM
Net Income	-22.0%	26.4%	78.8%	NM	-43.7%	-106.9%	NM	82.0%
Operating EPS		-27.4%	73.7%	NM	-52.7%	-106.6%	NM	75.6%

* Operating EPS excludes non-recurring one time items (FAS 123R adjustments made for 2006 and future periods)

A = Actual; E = Citi Investment Research estimates

Source: Company Reports and CIR Estimates

F.T. Alexandra Mahaney, State Bar No. 125984
Natalie J. Morgan, State Bar No. 211143
WILSON SONSINI GOODRICH & ROSATI
Professional Corporation
12235 El Camino Real, Suite 200
San Diego, CA 92130
Telephone: (858) 350-2300
Facsimile: (858) 350-2399
Email: amahaney@wsgr.com

Bruce R. Genderson (admitted *pro hac vice*)
Aaron P. Maurer (admitted *pro hac vice*)
Rachel Shanahan Rodman (admitted *pro hac vice*)
Adam D. Harber (admitted *pro hac vice*)
WILLIAMS & CONNOLLY LLP
725 Twelfth St. NW
Washington, DC 20005
Telephone: (202) 434-5000
Facsimile: (202) 434-5029

Attorneys for Defendant and Counterclaimant
SENORX, INC.

UNITED STATES DISTRICT COURT

NORTHERN DISTRICT OF CALIFORNIA

SAN JOSE DIVISION

HOLOGIC, INC., CYTYC CORPORATION and HOLOGIC L.P., Plaintiffs, v. SENORX, INC., Defendant.	Case No. C-08-0133 RMW (RS) **DEFENDANT AND COUNTERCLAIMANT SENORX, INC.'S NOTICE OF MANUAL FILING**
SENORX, INC., Counterclaimant, v. HOLOGIC, INC., CYTYC CORPORATION and HOLOGIC L.P., Counterdefendants.	

Regarding: **Exhibits 33, 36, 37 and 40 to the Declaration of Adam D. Harber In Support Of Defendant Senorx, Inc.'s Opposition To Plaintiffs' Motion For A Preliminary Injunction - Submitted Pursuant To Permission Granted At Hearing Of April 21, 2008.**

This filing is in paper or physical form only, and is being maintained in the case file in the Clerk's office. If you are a participant in this case, this filing will be served in hard-copy shortly. For information on retrieving this filing directly from the court, please see the court's main web site at http://www.cand.uscourts.gov under Frequently Asked Questions (FAQ).

This filing was not efiled for the following reason(s):

[X] Item(s) Under Seal

Dated: April 23, 2008

Respectfully submitted,

By: s/Natalie J. Morgan

F.T. Alexandra Mahaney, State Bar No. 125984
WILSON SONSINI GOODRICH & ROSATI
Professional Corporation
12235 El Camino Real, Suite 200
San Diego, CA 92130
Telephone: (858) 350-2300
Facsimile: (858) 350-2399
Email: amahaney@wsgr.com

Bruce R. Genderson (admitted *pro hac vice*)
Aaron P. Maurer (admitted *pro hac vice*)
Rachel Shanahan Rodman (admitted *pro hac vice*)
Adam D. Harber (admitted *pro hac vice*)
WILLIAMS & CONNOLLY LLP
725 Twelfth St. NW
Washington, DC 20005
Telephone: (202) 434-5000
Facsimile: (202) 434-5029

Attorneys for Defendant and Counterclaimant
SENORX, INC.

CERTIFICATE OF SERVICE
U.S. District Court, Northern District of California,
Hologic, Inc. et al. v. SenoRx, Inc.
Case No. C-08-0133 RMW (RS)

I, Liz Bojorquez, declare:

I am and was at the time of the service mentioned in this declaration, employed in the County of San Diego, California. I am over the age of 18 years and not a party to the within action. My business address is 12235 El Camino Real, Ste. 200, San Diego, CA, 92130.

On April 23, 2008, I served a copy(ies) of the following document(s):

DEFENDANT AND COUNTERCLAIMANT SENORX, INC.'S NOTICE OF MANUAL FILING

on the parties to this action by placing them in a sealed envelope(s) addressed as follows:

Henry C. Su (suh@howrey.com) Katharine L. Altemus (altemusk@howrey.com) HOWREY LLP 1950 University Avenue, 4th Floor East Palo Alto, CA 94303 Telephone: (650) 798-3500 Facsimile: (650) 798-3600	Attorneys for Plaintiffs HOLOGIC, INC. CYTYC CORPORATION and HOLOGIC LP
Matthew Wolf (wolfm@howrey.com) Marc Cohn (cohnm@howrey.com) HOWREY LLP 1229 Pennsylvania Avenue, NW Washington, DC 20004 Telephone: (202) 783-0800 Facsimile: (202) 383-6610	Attorneys for Plaintiffs HOLOGIC, INC. CYTYC CORPORATION and HOLOGIC LP

☐ (BY MAIL) I placed the sealed envelope(s) for collection and mailing by following the ordinary business practices of Wilson Sonsini Goodrich & Rosati, 12235 El Camino Real, Ste. 200, San Diego, CA. I am readily familiar with WSGR's practice for collecting and processing of correspondence for mailing with the United States Postal Service, said practice being that, in the ordinary course of business, correspondence with postage fully prepaid is deposited with the United States Postal Service the same day as it is placed for collection.

☒ (BY ELECTRONIC MAIL) I caused such document(s) to be sent via electronic mail (email) to the above listed names and email addresses.

☐ (BY PERSONAL SERVICE) I caused to be delivered by hand to the addressee(s) noted above. I delivered to an authorized courier or driver to be delivered on the same date. A proof of service signed by the authorized courier will be filed with the court upon request.

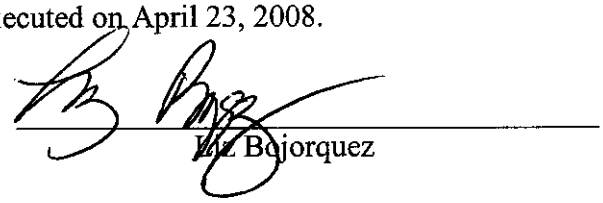
☐ (BY OVERNIGHT DELIVERY) I placed the sealed envelope(s) or package(s), to the addressee(s) noted above, designated by the express service carrier for collection and overnight delivery by following the ordinary business practices of Wilson Sonsini Goodrich & Rosati, 12235 El Camino Real, Ste. 200, San Diego, CA. I am readily familiar with WSGR's practice for collecting and processing of correspondence for

overnight delivery, said practice being that, in the ordinary course of business, correspondence for overnight delivery is deposited with delivery fees paid or provided for at the carrier's express service offices for next-day delivery the same day as the correspondence is placed for collection.

☐ (BY FACSIMILE) I caused to be transmitted by facsimile machine (number of sending facsimile machine is (858) 350-2399 at the time stated on the attached transmission report(s) by sending the documents(s) to (see above). The facsimile transmission(s) was/were reported as complete and without error.

☒ (BY CM/ECF) I caused such document(s) to be sent via electronic mail through the Case Management/Electronic Case File system with the U.S. District Court for the Northern District of California.

I declare under penalty of perjury under the laws of the United States that the above is true and correct, and that this declaration was executed on April 23, 2008.



Liz Bojorquez